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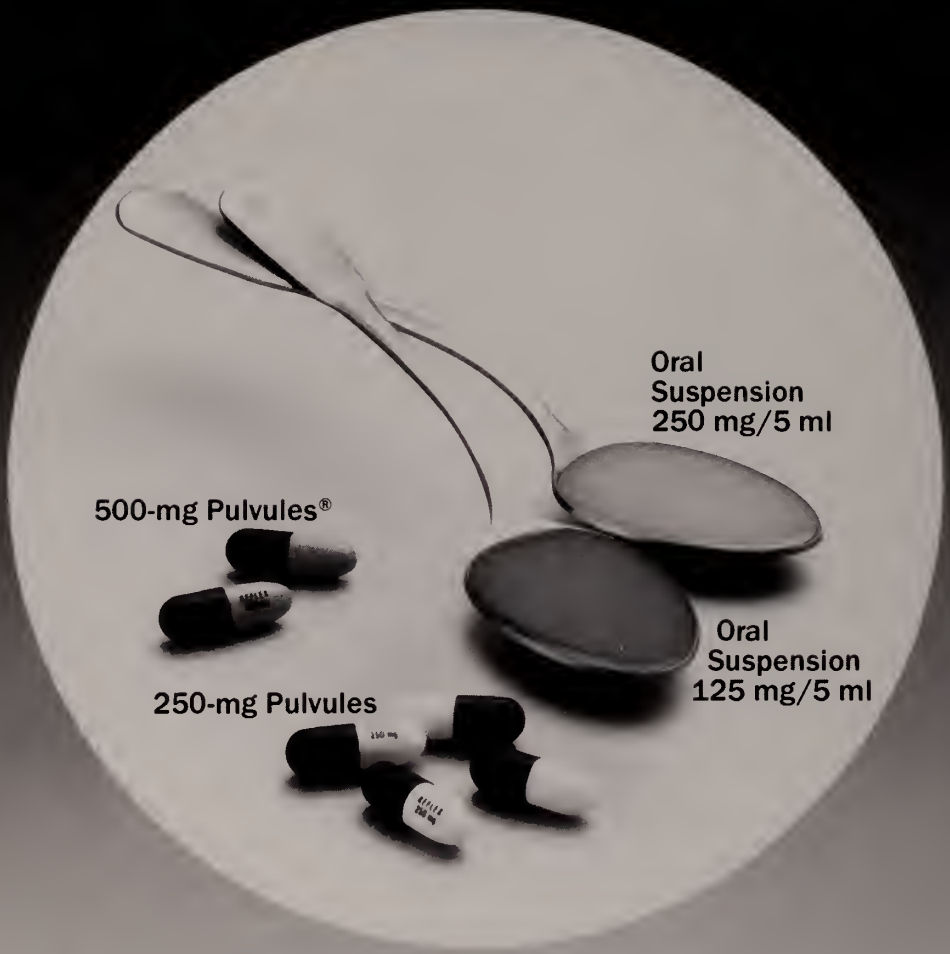

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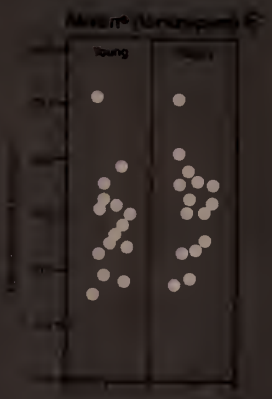

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Brief Summary of Prescribing Information.

Indications and Usage: Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic.

Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

Contraindications: Known sensitivity to benzodiazepines or acute narrow-angle glaucoma.

Warnings: Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

Physical and Psychological Dependence: Withdrawal symptoms like those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, e.g. drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months.

Precautions: In depression accompanying anxiety, consider possibility for suicide.

For elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Terminate dosage gradually since abrupt withdrawal of any antianxiety agent may result in symptoms like those being treated: anxiety, agitation, irritability, tension, insomnia and occasional convulsions. Observe usual precautions with impaired renal or hepatic function. Where gastrointestinal or cardiovascular disorders coexist with anxiety, note that lorazepam has not been shown of significant benefit in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 6 times maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment was withdrawn within 2 months of first observation. Clinical significance is unknown; but use of lorazepam for prolonged periods and in geriatrics requires caution and frequent monitoring for symptoms of upper G.I. disease. Safety and effectiveness in children under 12 years have not been established.

ESSENTIAL LABORATORY TESTS: Some patients have developed leukopenia; some have had elevations of LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

CARCINOGENESIS AND MUTAGENESIS: No evidence of carcinogenic potential emerged in rats during an 18-month study. No studies regarding mutagenesis have been performed.

PREGNANCY: Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although all these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of discontinuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

NURSING MOTHERS: It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

Adverse Reactions, if they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%) and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbance, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and unsteadiness increased with age. Small decreases in blood pressure have been noted but are not clinically significant, probably being related to relief of anxiety.

Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

Overdosage: In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce vomiting and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol Bitartrate Injection U.S.P. Usefulness of dialysis has not been determined.

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AROUND THE STATE

MANHATTAN

Feb 2–4. **Bioregulatory Functions of Thrombin.** Barbizon-Plaza Hotel. Info: Conference Director, The New York Academy of Sciences, 2 East 63 St, New York, NY 10021.

Feb 6–8. **Surgical Courses in Lens Implantation.** Info: Ruth Green, Administrator, Ophthalmological Foundation of America, 823 United Nations Plaza, New York, NY 10017. Tel: (212) 986-4848.

BRONX

Feb 21. **Resuscitative Thoracotomy: The Use of Open Chest Resuscitation in Traumatic and Non-Traumatic Cardiac Arrest.** Info: Office of Medical Education, 2A5, Lincoln Hospital, 249 East 149 St, Bronx, NY 10451. Tel: (212) 830-1305.

QUEENS

Feb 19. **16th Annual Pediatric Board Review Course: 1986.** Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

BROOKLYN

Feb 5. **HLA and Human Disease.** *Feb 12.* **Current Management of Hemophilia and von Willebrand Disease.** *Feb 19.* **Human Tumor Markers.** *Feb 26.* **AIDS: Implications for Transfusion and Blood Banking.** Info: Division of Hematology/Oncology, Department of Medicine, Interfaith Medical Center, 555 Prospect Pl, Brooklyn, NY 11238. Tel: (718) 240-1211.

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Feb 5. **Life Threatening Arrhythmias—New Oral Drugs.** *Feb 19.* **Practical Approaches to Acid-Base Disturbances.** Info: Medical Education Department, Mercy Hospital, 1000 North Village Ave, Rockville Centre, NY 11570. Tel: (516) 255-2260.

Feb 7. **Gynecology for the Non-Gynecologist.** *Feb 28.* **Treatment of Wilm's Tumor.** Info: Medical Staff Office, Long Beach Memorial Hospital, 455 East Bay Dr, Long Beach, NY 11561. Tel: (516) 432-8000, ext. 2275.

Feb 11. **Supraventricular Tachycardia.** 1 Cat 1 Credit. *Feb 25.* **Cardiac Arrest Management.** 1 Cat 1 Credit. Info: The Community Hospital at Glen Cove, St. Andrews La, Glen Cove, NY 11542. Tel: (516) 676-5000.

Feb 28. **Update in Ophthalmology.** 6 Cat 1 Credits. Info: Elsa Rahn, MD, Division of Ophthalmology, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-2706.

SUFFOLK

Feb 4. **Evaluation of the Child with Failure to Thrive.** *Feb 11.* **Renal: Urinary Tract Infections.** *Feb 18.* **Neurology: Seizure Disorders in Children.** Info: Arthur J. Schwager, MD, Director, Continuing Pediatric Medical Education, Huntington Hospital, Park Ave, Huntington, NY 11743.

ROCKLAND

Feb 4. **Pituitary Adenoma.** *Feb 18.* **Metabolic Bone Disease.** 1 Cat 1 Credit. Info: Myrna Hahn, Nyack Hospital, N. Midland Ave, Nyack, NY 10960. Tel: (914) 358-6200, ext. 2509.

AROUND THE NATION

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Feb 7–8. **Otolaryngology: "Hands On" Experience.** Info: The Western Institute for Laser Treatment, 2320 Bath St, Suite 207, Santa Barbara, CA 93105. Tel: (805) 682-6061.

Feb 13–15. **Recent Advances in Neurology.** 15 Cat 1 Credits. Info: Extended Programs in Medical Education, Registration Office, 569-U, University of California, San Francisco, CA 94143. Tel: (415) 476-4251.

COLORADO

Feb 15–22. **Third Annual Rheumatology Conference.** 22 Cat 1 Credits. Marriott's Mark Resort, Vail. Info: Vail University Conference, PO Box 11338, Denver, CO 80211-0338. Tel: (303) 629-5333.

FLORIDA

Feb 2–4. **Endoscopic Laser Therapy Update.** *Feb 5–7.* **Computers for the Practicing Physician: Update 1986.** *Feb 7–9.* **Pediatric Radiology in the Emergency Room.** Contemporary Resort at Walt Disney World. Info: Department of Continuing Medical Education, Boston University School of Medicine, 80 East Concord St, Boston, MA 02118. Tel: (617) 638-4605.

Feb 16–19. **Magnetic Resonance Imaging Update.** 18 Cat 1 Credits. Hyatt Palm Beaches. Info: Department of Continuing Medical Education, Boston University School of Medicine, 80 East Concord St, Boston, MA 02118. Tel: (617) 638-4605.

Feb 28–Mar 1. **Pediatrics.** 15 Cat 1 Credits. Sheraton Bal Harbour Hotel. Info: Rayna Saville, Coordinator, Pediatric Continuing Medical Education, Children's Hospital of Buffalo, 219 Bryant St, Buffalo, NY 14222. Tel: (716) 878-7630.

KENTUCKY

Feb 23–28. **17th Family Medicine Review.** Hyatt Regency Hotel. Info: University of Kentucky College of Medicine, Office of Continuing Education, 132 COM Office Building, Lexington, KY 40536-0086. Tel: (606) 233-5161.

LOUISIANA

Feb 14–15. **Symposium on Cataract: Biochemical, Medical, Surgical, Laser.** 14 Cat 1 Credits. Sheraton New Orleans Hotel. Info: Symposium Director, The Eye Foundation of America, 823 Maison Blanche Building, New Orleans, LA 70112. Tel: (504) 581-3714.

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The dilemma of "do not resuscitate" orders

In recent years technologic advances have made it relatively easy to extend the precise moment of death, yet physicians continue to be confronted by a host of conditions that are irreversible and that all too frequently are associated in their final stages with torment for patient and family alike. The Veterans Administration has acknowledged that ". . . in some instances therapeutic treatment and the application of medical technology may not cure a disease or reverse a patient's course, and patients who are incurable may reach a point where . . . additional measures would become not only unwarranted but medically unsound."[1] Organs are not transplanted when the patient is known to have widespread malignancy. Performing cardiac bypass surgery on a patient who has leukemia in addition to cardiac disease would be criminal—figuratively, if not literally. There is a fundamental principle that therapeutic measures, including cardiopulmonary resuscitation, are not indicated merely because they are available. Their appropriateness in any individual case must be determined on the basis of many factors.

Cardiopulmonary resuscitation, initially developed for otherwise healthy persons whose heart beat and breathing failed following surgery or near drowning, is now applied almost as a routine to any person who has a cardiac arrest in a hospital.[2] Whether, when, by whom, and how a decision should be made not to resuscitate a patient after cardiac arrest are complex questions that, by definition, have life and death significance. They can be considered from many perspectives, but ultimately it is the clinical perspective that should affect the decision to resuscitate a patient. As difficult as the clinical considerations may be, the administrative and legal ramifications regarding cardiopulmonary resuscitation are even more challenging.

The premises underlying "do not resuscitate" (DNR) policies should be the same as those that guide other areas of clinical decision-making. The physician's primary obligation is to his or her patient: to educate, to treat, and to be an advocate for that individual.[3] The physician has the ability to recognize the complexity of illness and the options for treatment, but it is the patient, when competent, who must have a decisive voice regarding the care that is to be rendered. Accordingly, when a patient has directed that resuscitation *not* be instituted, a DNR order to implement that directive is necessary and appropriate.

Once the diagnosis of a terminal, progressive, or irreversible illness has been made, the physician should take the initiative in raising the subject of resuscitation in the event of cardiopulmonary arrest. It is essential to do so for the severely ill, hospitalized patient to avoid subjecting such patients to unnecessary and futile resuscitative efforts. The assumption that all persons expect and demand maximal care is refuted when patients are questioned. Even among the relatively small cohort of survivors of cardiopulmonary resuscitation—those who are discharged from the hospital and are still alive six months after successful resuscitation—about one half state that they would not wish to have resuscitation performed in the future.[4] In a related study, it was demonstrated that physicians who rely on "signals" or intuition to determine the patient's preference in the event of cardiac arrest are deluding themselves.[5]

The physician is required by both ethical canons and legal mandate to respect an adult patient's right to refuse treatment, even when that treatment is deemed to have life-or-death consequences. However, many members of the medical profession believe that they may not honor an unequivocal directive by a patient that he or she does not wish to be resuscitated in the event of cardiac arrest. This leads to the paradox whereby a patient has the right to refuse life-saving treatment, but is unable to forbid measures to postpone, however briefly, the death that is a consequence of such a refusal.

The issues are far more complex when the patient is believed to be non compos mentis and unable to make an informed decision regarding his or her medical care. The family is traditionally called on to participate in deliberations regarding the therapeutic management of incapacitated patients. Although recent court decisions in New York[6] have cast doubt on the family's ability to refuse consent to medical care, there is no other practical way for providers to determine the appropriate management of patients in this situation. The family is often in the best position to express the wishes of an incompetent or unconscious patient. If the physician feels that these wishes are reasonable, then they should be respected. However, if a family wishes an incompetent patient not to be resuscitated and the wish of that patient is unknown, a DNR order should not be written if in the judgment of the physician it is inappropriate. In such instances consultation with the hospital ethics committee and legal counsel is advisable. It has been suggested that encouraging patients to prepare a written statement indicating their wishes regarding resuscitation is helpful in avoiding such a situation.[7]

There will be instances in which the physician feels the

wishes expressed by a patient are inconsistent with reasonable standards of medical practice, or are distasteful for ethical or moral reasons. A physician must be free to make the choice not to treat a patient if the constraints or demands made with respect to medical treatment are considered unacceptable. In such cases, however, there is a concomitant obligation on the part of the physician to arrange for referral to a colleague who is willing to accept the patient on the terms that have been stipulated.

Many hospitals have yet to adopt guidelines acknowledging a role for "do not resuscitate" orders and describing the manner in which such orders are to be recorded and acted upon.[8] Compounding the widespread inability of institutions to accept and accommodate this therapeutic imperative, many physicians are reluctant to initiate discussions with patients regarding the institution of life support, even when clinical judgment dictates unequivocally that resuscitative measures are contraindicated. At the same time, some physicians ask the patients' relatives to make the decision whether or not to resuscitate. Where there is a consensus among all the participants that a "do not resuscitate" order is acceptable, the physician *may* comply— depending on the degree of conviction of the physician, the hospital, and the attorneys for both. If consensus is lacking, then most patients will be subjected to resuscitation regardless of their own clearly expressed directive, and regardless of what their physician believes to be clinically indicated considering the nature of the illness and its prognosis. Alternatively, there will be tacit and undocumented agreements among hospital staff to engage in "show-codes" (sham efforts to resuscitate), or "slow-codes" (resuscitation measures purposefully carried out in a manner so slow as to preclude success).

What is the basis for this situation? Why is a practice clearly defined by New York law[9] as unprofessional conduct—imposing treatment that is unnecessary or rejected by the patient—tolerated in the case of physicians caring for the terminally ill? The answer is that it is the perceived threat of civil and criminal penalties associated with doing what medical and ethical considerations indicate is appropriate. The fact is, however, that the threat of challenge by a plaintiff or prosecutor cannot be eliminated regardless of the course one chooses to follow. This being the case, the response to the conflict must be that the patient's interests be given priority over all other considerations, including the advice of counsel. This conclusion reflects the conviction that health care providers and their patients will be served best if physicians and hospital administrators resolve medical and legal dilemmas that defy compromise by sticking to that which they know best: medicine, and not the law.

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Not enough is enough

The physician who is dependent on alcohol and other drugs

Like most illnesses, chemical dependence can affect all people, including physicians. However, there are no statistics presently available comparing the incidence of chemical dependence among physicians as with other Americans. Lacking such specific studies, it is reasonable to project from the estimated 10% prevalence of alcohol dependence in the general population of drinkers that there are at least 4,000 who are chemically dependent among the 60,000 physicians licensed by New York State.[1] Chemical dependence among physicians tends to skew toward opioids and sedative drugs, other than alcohol, as seen from data collected in New Jersey.[2]

It is difficult for physicians dependent on mind- and mood-altering chemicals to acknowledge their illness or seek treatment without encouragement. Usually it is not until progressive behavioral deterioration becomes obvious to family or colleagues that the individual seeks assistance. Even then, through misjudgments related either to

the toxic effect caused by any of these various chemicals or to addiction to those chemicals, many physicians continue their substance abuse. Such physicians often will either leave or curtail practice rather than seek help.

Although continued recovery after treatment for chemical dependence is not certain, physicians who follow a structured rehabilitation program with continued participation in a self-help recovery group such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) have a 77%[3] to 100%[4] chance for recovery. The rate of recovery for physicians exceeds that for treated populations in general.

There are several other factors that may interfere with a physician seeking treatment for substance abuse. Dependent physicians deny that their illness has reduced their ability to practice medicine or interact socially. Part of the psychologic dysfunction from the illness is the increasing inability of the physician to conceptualize and think in an abstract manner. This in turn leads to rumination and self-recrimination as the illness progresses, making it difficult for the physician to seek treatment for the dependence. Over time the responsibility of obtaining treatment for an impaired physician often shifts to family, friends, and concerned colleagues.

Confronting an ill colleague, spouse, or parent is a difficult task. However, a physician's hope for rehabilitation usually lies with someone in the family or a close colleague. The success of an initial confrontation depends on the respect and concern for the impaired individual shown during the confrontation. By moralizing or being judgmental, one lessens the chances for a successful outcome of an intervention.

Although the initial confrontation by someone close to a chemically-dependent physician often fails to result in immediate treatment, it may eventually lead to the beginning of recovery. It is wise to follow an initial confrontation that has failed with a more structured and formal confrontation conducted by an individual qualified by training and experience. That secondary intervention more likely will also lead to treatment and recovery.

Among the primary concerns of the Committee for Physicians' Health (CPH) of the Medical Society of the State of New York is the early detection and treatment of chemically-dependent physicians. Most often the CPH is informed of a chemically-dependent physician by family, friends, and colleagues. It is imperative that these ill physicians be referred to the CPH before deterioration progresses to the point where punitive measures are necessary to protect the patients of the physician from possible professional misconduct. However, if the illness is suspected in an early stage, it is difficult to be confident about that suspicion. Therefore, members of the committee are available to help clarify such a situation.

The following is a list of possible characteristics that may be recognized by persons referring impaired physicians to the CPH:

- Disruptions in family life.
- The development of legal problems.
- Neglectful of practice routines.
- Social isolation.
- Driving while intoxicated.
- Intoxication while attending social functions.
- Noticeable odor of alcohol at the worksite.
- Making hospital rounds at unusual times.
- Cancelling office appointments without obvious conflict of time.
- Giving unusual or dangerous orders over the telephone, particularly from home during the evening or night.
- Disruptive behavior at meetings, or failure to complete committee assignments.
- Forgetting social appointments.
- Holding telephone conversations with slurred speech or tangential conversation.
- Dressing sloppily, or in a noticeably different style.

Self-referral and referral from others to the CPH program is often delayed by the concern that the individual suffering from a socially stigmatizing disease may lose his or her anonymity. Unless a physician is an imminent danger to patients or has already injured a patient, the CPH is careful about protecting the individual's anonymity from any person or agency outside of the program, unless the physician has signed a consent for such communication.

If left untreated, chemical dependence is a progressive and destructive illness. Early intervention prevents the accumulation of increasingly severe and potentially irreversible consequences for the physician's physical health, mental health, and social welfare. The most caring and constructive act from any potential referral source is early referral to the CPH. An almost universal reaction of physicians in recovery from chemical dependence is gratitude for intercession, regardless of how much they resisted diagnosis and treatment during their illness.

In addition to helping identify and guide the impaired physician into acceptable and appropriate treatment, the CPH assumes responsibility for monitoring the physician for at least two years after treatment while the significant possibility of relapse, though diminishing, is present. Also the CPH advocates when necessary the return of a medical license or reinstatement on a hospital staff during reentry into practice for those clearly in recovery.

An integral part of the traditions among physicians is finding help for colleagues who are ill. Physicians are responsible for finding treatment for their chemically-dependent colleagues for maintaining the integrity of the profession, and for protecting patients from substandard care.

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Complaints of breathlessness in the emergency department

The experience at a community hospital

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ABSTRACT. The records of the Emergency Department of Rochester General Hospital were reviewed for a five-week period to determine the distribution of diagnoses associated with patients who were seen with the primary complaint of shortness of breath. The clinical characteristics of those admitted to the hospital were compared to those patients treated and released. One hundred sixty-two patients with a primary complaint of breathlessness were seen (2.7% of all Emergency Department visits). Eighty-four of the 162 patients (52%) were admitted, comprising 16% of all nonsurgical hospital admissions. Congestive heart failure, asthma, and chronic obstructive lung disease constituted 26%, 25%, and 15% of the diagnoses, respectively. A comparison of patients who were admitted to those who were treated and released showed differences only in body temperature and blood gas values in chronic obstructive disease, pulse rate in congestive heart failure, and respiratory rate in asthma. Other clinical indices in these groups were similar, suggesting that factors other than simply quantifiable medical parameters were being used to make the decision to hospitalize a patient for treatment.

(NY State J Med 1986; 86:4-6)

Acute breathlessness is a symptom that frequently demands urgent medical attention. Therefore, many patients complaining of shortness of breath will come to the hospital emergency department for evaluation and treatment. Moreover, breathlessness is often an initial symptom of possible serious illness requiring inhospital care. Pearson and colleagues reported that 25% of all emergency admissions at the University Hospital of Nottingham, England presented with acute shortness of breath.[1]

The records for a five-week interval of all patients visiting the emergency department of a community hospital with a primary complaint of breathlessness were studied. The diagnoses of these patients were recorded and relevant clinical information available at the time the decision was made either to treat and release, or to admit the patient to the hospital for more prolonged care was tabulated.

This research defines the spectrum of disease occurring in patients complaining of breathlessness evaluated in the emergency department, and compares the clinical characteristics of those patients admitted to those treated and released in order to determine what factors prompt physicians to make this important decision.

PATIENTS AND METHODS

Rochester General Hospital, a 547-bed community hospital, is one of six hospitals serving metropolitan Rochester, NY (1980 population, 730,000).[2] The Emergency Department is staffed by medical and surgical residents and eight full-time physicians, five of whom have been trained in surgery, and three of whom have internal medicine training. None of these full-time physicians have specialty training in emergency medicine.

All of the records of patients seen in the Emergency Department for a five-week period were screened, and the records of patients with a primary complaint of shortness of breath were carefully examined. Demographic, historic, physiologic, and laboratory values were analyzed, and the diagnosis was recorded.

TABLE I. Diagnoses of Patients Complaining of Breathlessness

Diagnosis	No. of patients	Age* (yr)	Admitted(%)†
Congestive heart failure	42	72.2 ± 10.8	74%
Asthma	41	29.0 ± 23.0	24%
Chronic obstructive lung disease	24	69.4 ± 6.3	71%
Acute infection			
Pneumonia	5	64.0 ± 29.1	60%
Bronchitis	7	49.4 ± 29.0	0%
Croup	5	2.0 ± 1.4	20%
Myocardial infarction	9	71.9 ± 8.3	100%
Hyperventilation	7	21.7 ± 10.0	0%
Other‡	22	54.1 ± 21.3	59%

* Values are mean ± SD.
† Percent admitted to hospital.
‡ See text for diagnoses.

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TABLE II. Clinical Variables for Admitted and Not Admitted Patients with the Diagnosis of Chronic Obstructive Pulmonary Disease

	Admitted	Not admitted
Number of patients	17	7
Age (yr)	69.5 ± 6.1*	69.3 ± 7.3
Acute symptom duration (d)	4.2 ± 4.5	4.3 ± 4.8
Pulse rate (beats/min)	109.6 ± 19.2	99.7 ± 27.1
Respiratory rate (breaths/min)	32.7 ± 7.4	29.4 ± 8.5
Wheezing by auscultation (%)	65%	57%
Peripheral edema (%)	35%	14%
Body temperature (C°)	37.8 ± 1.1	36.8 ± 0.5†
Arterial blood pH	7.35 ± 0.08	7.44 ± 0.06†
Arterial blood pH <7.30 (%)	29%	0%
Arterial blood P_{CO_2} (mm Hg)	50.8 ± 14.4	33.5 ± 13.3†
Arterial blood P_{O_2} (mm Hg)	46.9 ± 17.7	65.8 ± 24.5†
White blood cell count (leukocyte count/1000)	10.6 ± 4.2	8.9 ± 1.2

* Values are mean ± SD.
† Values differ at $P < .05$ level.

Statistical analysis was by *t*-test for groups of unequal size and by analysis of proportion.[3]

Results

One hundred sixty-two of 6,005 patients (2.7%) seen in the Emergency Department during the study period had a primary complaint of shortness of breath. Eighty-four (52%) of these patients were admitted, comprising 16% of all patients admitted to nonsurgical services; 27 of these 84 admissions were to intensive care areas. The mean age (±SD) for the 162 patients was 52.8 ± 26.8 years, with a range of ten months to 95 years. Those below the age of 20 years comprised 18.5% of patients seen and 5% of admissions; those aged 21 to 69 years comprised 43.2% of patients seen and 40% of admissions; and those 70 years of age and older comprised 38.3% of patients seen and 55% of admissions. Sixty percent (98 of 162) of the patients were men.

Table I classifies the patients studied by diagnosis, and shows the mean age and percent admitted in each diagnostic group. The category "Other" included patients with musculoskeletal chest pain, 3; lung carcinoma, 4; occluded permanent tracheotomy, 2; anemia, 1; pneumothorax, 1; pulmonary embolus, 1; pleural effusion, 1; tachyarrhythmia without congestive heart failure, 2; angina, 3; diabetic ketoacidosis, 1; sickle cell crisis, 1; and central nervous system disease, 2. The category "Myocardial infarction" included only those patients who had breathlessness as a major complaint. For classification purposes, the category "Bronchitis" did not include patients having underlying chronic obstructive lung disease. Patients with acute bronchitis exacerbating chronic obstructive lung disease were classified in the "Chronic obstructive pulmonary disease" category.

The percentage of patients admitted to the hospital from each diagnostic category ranged from 0% of those with hyperventilation syndrome or acute bronchitis to 100% of those with myocardial infarction.

Table II examines variables that were recorded for patients with chronic obstructive lung disease, comparing those patients admitted to those treated and released. Those admitted had higher body temperatures, lower pH and P_{O_2} values and higher P_{CO_2} values than those treated and released. Age, duration of breathlessness, heart rate, respiratory rate, and the presence or absence of edema and wheezing was not different between the two groups.

Table III examines variables for patients with congestive heart failure. Admitted patients had a higher heart rate than those treated and released. Age, duration of breathlessness, systolic and diastolic blood pressures, respiratory rate, the presence of rales, peripheral edema, radiographic evidence of alveolar pulmonary edema, and arterial blood gas values were not significantly different between those patients admitted and those not admitted in this diagnostic group.

Among patients with asthma (Table IV), the respiratory rate was higher in those admitted than in those treated and released. Age, duration of breathlessness, heart rate, the presence of wheezing, the use of accessory muscles, and arterial blood gas values were not different. Pulsus paradoxus and expiratory flow rates were not measured often enough to allow valid comparison.

Discussion

Breathlessness was a condition that accounted for 162 visits in a five-week period to a 547-bed community hospital serving a large geographic area. Although this number is a small fraction of the 6,005 patient visits to the Emergency Department in that interval, it included patients who comprised 16% of nonsurgical admissions from the Emergency Department. This figure is similar to the 25% reported from Nottingham, England,[1] and the 21% from Carlisle, England,[4] reflecting the seriousness of the condition and the impact of these patients on hospital resources.

Although this study was performed in 1982, there have been no factors that have occurred in the patient population or Emergency Department practice of this hospital that would alter the results. The delay in submission of the material is explained by the project being a summer medical student research elective, which prolongs the analysis of data and preparation of the text because of the many time commitments and responsibilities involved in medical school education.

The diagnoses of asthma and congestive heart failure each comprised approximately 25% of the total study group, and chronic obstructive lung disease comprised 15%. Acute respiratory infection, myocardial infarction, and hyperventilation syndrome combined comprised another 20%, and a wide variety of other diagnoses comprised the remainder. The distribution of the most common emergency diagnoses of dyspneic patients reported here was similar to that reported by Mustchin and Tiwari, where pulmonary edema comprised 30%, asthma 20%,

TABLE III. Clinical Variables for Admitted and Not Admitted Patients with the Diagnosis of Congestive Heart Failure

	Admitted	Not admitted
Number of patients	31	11
Age (yr)	72.5 ± 10.9*	71.9 ± 10.5
Acute symptom duration (d)	2.8 ± 4.06	3.2 ± 3.9
Pulse rate (beats/min)	106.5 ± 20.1	89.4 ± 14.6†
Respiratory rate (breaths/min)	29.3 ± 7.6	29.2 ± 7.4
Blood pressure (mm Hg)	147 ± 39/ 88.3 ± 21.5	155.5 ± 41.7/ 93.3 ± 12.9
Peripheral edema (%)	26%	44%
Rales by auscultation (%)	100%	91%
Alveolar edema on chest radiograph (%)	29%	18%
Arterial blood pH	7.32 ± 0.16	7.37 ± 0.15
Arterial blood pH <7.30 (%)	26%	18%
Arterial blood P_{CO_2} (mm Hg)	44.0 ± 16.3	41.2 ± 12.0
Arterial blood P_{O_2} (mm Hg)	64.2 ± 22.9	68.2 ± 19.5

* Values are mean ± SD.
† Values differ at $P < .05$ level.

TABLE IV. Clinical Variables for Admitted and Not Admitted Patients with the Diagnosis of Asthma

	Admitted	Not admitted
Number of patients	10	31
Age (yr)	31.8 ± 21.8*	27.4 ± 23.6
Acute symptom duration (d)	2.6 ± 4.7	1.9 ± 2.6
Pulse rate (beats/min)	108.2 ± 17.8	109.1 ± 20.1
Respiratory rate (breaths/min)	40.1 ± 11.1	32.1 ± 10.3†
Wheezing by auscultation	100%	97%
Accessory muscle use	30%	35%
Arterial blood pH‡	7.38 ± 0.11	7.38 ± 0.04
Arterial blood P_{CO_2} (mm Hg)‡	38.9 ± 8.2	40.3 ± 7.5
Arterial blood P_{O_2} (40 mm Hg)‡	20%	10%
Arterial blood P_{CO_2} (mm Hg)‡	63.7 ± 11.9	64.0 ± 14.3

* Values are mean ± SD.
† Values differ at $P < .05$ level.
‡ Six of ten patients admitted and six of 31 patients not admitted had arterial blood gases obtained.

and chronic airway obstruction 17% of a study group.[4] This similarity suggests that the experience reported here is not atypical and represents the distribution of diagnoses seen in other hospitals.

Only a few relevant clinical parameters were significantly different between the admitted patients and those that were treated and released in the Chronic obstructive pulmonary disease, Heart failure, and Asthma groups. The difficulty in finding many objective differences between patients admitted and those treated and released is seen also in the experience of Kelsen and associates[5] in their assessment of asthmatics. Fischl and coworkers[6] derived a multivariable predictive index, and Zwicke and colleagues[7] utilized an observation unit to more accurately predict those asthmatics who would need hospital admission. These protocols were not used in the patients with asthma in the study reported here and protocols of similar nature were not available for the evaluation of patients with chronic obstructive lung disease and congestive heart failure. Moreover, the predicting index of Fischl and associates could not be confirmed in a subsequent study from another institution,[8] raising doubts about the utility of the index in actual practice or in different clinical settings.

Since the financial and medical risks of inappropriate hospital admission or nonadmission are great, it seems warranted to carefully investigate criteria by which these decisions are made. If pertinent medical variables discriminate poorly between those patients admitted and those treated and released, then identification of the important nonmedical variables is necessary. Such variables might include the home environment of the patients, their emotional capacity to cope with an acute illness or to manage it at home, family demands, physicians' recent or remote experiences with similar patients, or their subjective assessment of the degree of illness. These and other variables are subtle and may be difficult to identify and quantify; hence they may not be appreciated or utilized in clinical analysis or peer-review evaluations. In addition, reimbursement defined by categories such as Diagnostic Related Groupings (DRGs) cannot readily take into account these important social factors. This is especially true when the patient population deviates from that which has been used to define costs and length of stay for DRG purposes. Such populations might include those using emergency departments in older metropolitan areas in the northeastern United States, possibly with a disproportionate representation of poor, elderly, socially maladapted, or chronically ill individuals.

Any studies or guidelines, therefore, that propose to assess or define standards for admission, care, or reimbursement based on medical parameters only may seriously underestimate the complexity of medical practice in the emergency care of patients with dyspnea and perhaps with other disorders as well. This is likely to be true particularly if health, or the ability to maintain a state of well-being is understood to be more than a simple combination of physiologic and laboratory parameters.

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Bile duct cancer and cardiac anomalies

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ABSTRACT. A review of the incidence of biliary tract cancer at Columbia-Presbyterian Medical Center in New York City over the past forty years has revealed an apparent increase of cardiac anomalies among these cases as compared to the overall autopsy population. Therefore it has been suggested that an association may exist between these two conditions. However the conclusions drawn from this study must be viewed as tentative considering the limited scope of the investigation. Further research is necessary in order to more closely associate the incidence of cardiac anomalies with bile duct cancer.

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The incidence of cancer of the biliary tract as determined on autopsy for the past forty years at Columbia-Presbyterian Medical Center in New York City has recently been reviewed.[1,2] Although this type of cancer accounts for less than 1% of all malignancies, it is the fifth most common cancer of the digestive tract and represents approximately 4,500 deaths in this country per year. The average annual age-adjusted incidence rates for biliary tract cancer per 100,000 population range from approximately one for black men to greater than nine for American Indian women.[1-3]

Although a significant number of cancers arise throughout the biliary tract—including the intra- and extra-hepatic ducts and the ampulla of Vater—most of these tumors occur in the gallbladder, and most are well-differentiated adenocarcinomas. The association of biliary tract cancer with gallstone disease and certain occupational and environmental exposures has been noted[1-3] and most of the prior findings were compatible with previously reported results.[1,2]

In a previous report of extra-hepatic bile duct cancer the frequent occurrence of congenital cardiac anomalies was noted in passing.[2] Cases of intra-hepatic bile duct cancer have now been examined as well, and a similar frequent occurrence of cardiac anomalies has been found. Furthermore, the incidence of these anomalies in these cases has now been compared with the background autopsy population, and a previously unreported statistically significant increased incidence of various cardiac anomalies among these cases appears to have been found. It has been suggested that there may, in fact, be an association between cardiac anomalies and bile duct cancer on the basis of these observations.

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PATIENTS AND METHODS

All necropsy cases of cancer of the biliary tract at Columbia-Presbyterian Medical Center over the past forty years were ascertained from autopsy records, totalling greater than 80 cases of biliary tract cancer. These cases were then segregated by site of origin within the biliary tree (ie, gallbladder, extra-hepatic bile ducts, intra-hepatic bile ducts, or ampulla of Vater). The series contained 43 cases of gallbladder cancer and 11 cases of ampullary cancer. The remaining cases included 22 instances of extra-hepatic bile duct carcinoma and 11 instances of intra-hepatic bile duct carcinoma.

In each case, particular note was made of the presence of congenital anomalies—especially involving the heart—and the presence of second synchronous or metachronous malignancies. The cases of bile duct cancer were compared with the background autopsy population at the same medical center.[1] The characteristics of this background population were derived from a sample of all autopsy cases; the sample consisted of all cases to come to autopsy at this institution in the first and last five years of the study period (>2,000 cases).

The same standardized protocol for obtaining information was used for the control population as for the biliary cancer cases; specifically, the presence of congenital anomalies and second malignancies was noted when reviewing the records of the control population. Statistical analysis was performed using either the standard calculation of the critical ratio for inference on proportions (Z_c), or Fisher's exact test if the sample numbers were small enough to compromise the validity of the approximate test.[4] Statistical significance was assumed for P values less than 0.05.

RESULTS

Among 22 cases of extra-hepatic bile duct carcinoma there were five cases with cardiac anomalies; among 11 cases of intra-hepatic bile duct cancer there were four cases with cardiac anomalies. Of the total 33 cases of bile duct cancer, nine cases (27%) had cardiac anomalies. The anomalies noted were bicuspid aortic valve, quadricuspid tricuspid valve, anomalous coronary arteries, accessory coronary arteries, and atrial septal defects (Table). The cases with anomalies were not significantly different in terms of age or sex from those without; all of the tumors were relatively well-differentiated adenocarcinomas.

The exact reported incidence of cardiac anomalies at autopsy is difficult to determine. Literature estimates cover a broad range from less than 1% to greater than 8%.[5] The incidence of similar cardiac anomalies in the background autopsy population reported here was determined to be approximately 3%. However, the incidence of cardiac anomalies among the bile duct cases was greater (P <0.001). In fact, some of the anomalies noted among the bile duct cases, such as quadricuspid tricuspid valve, are quite rare and would not be expected to be seen in such a small series.

TABLE. Cases of Bile Duct Cancer with Cardiac Anomalies

Case no.	Bile duct cancer	Age/Sex	Cardiac anomaly
2	Extra-hepatic unclassified	84/F	Artial septal defect
17	Confluence of ducts	69/M	Quadricuspid tricuspid valve, bicuspid aortic valve
18	Common hepatic duct	70/M	Atrial septal defect, anomalous coronaries
19	Common bile duct	59/M	Anomalous and accessory coronaries
21	Left hepatic duct	59/M	Atrial septal defect
24	Intra-hepatic	39/F	Atrial septal defect
28	Intra-hepatic	48/F	Anomalous and accessory coronaries
30	Intra-hepatic	64/M	Atrial septal defect, accessory right coronary
31	Intra-hepatic	63/M	Atrial septal defect

The age and sex distribution of patients with biliary tract cancer at autopsy was similar to that for the control population at autopsy. The biliary cancer cases consisted of 58% men (average age, 63 years) and 42% women (average age, 62 years), with an overall average age of 62 years; the background population was made up of 54% men (average age, 60 years) and 46% women (average age, 60 years), with an overall average age of 60 years. The minor differences between biliary cancer cases and the background population in terms of age and sex are justified by the fact that bile duct cancer occurs more frequently in elderly men.[2,3] Correction for age and sex did not alter the statistical significance of these findings.

Discussion

There is a factual basis for the association observed in this study. In the embryologic setting the heart and bile ducts develop at about the same time in utero—approximately four to six weeks of gestation. Therefore, it is possible that common factors acting at that time could produce malformations or anomalies of both the heart and biliary tract. So-called arteriohepatic dysplasia syndromes have been reported by Watson and Miller[6] and Alagille and associates[7] linking biliary tract and cardiovascular malformations.

There has also been a reported association between certain biliary tract malformations and the development of cancer. Patients with Caroli's disease or congenitally dilated biliary tracts may be predisposed to malignancy due to prolonged exposure of bile duct epithelium to excreted carcinogens secondary to biliary stasis.[8-10] Therefore, patients with anomalies of the biliary tract might be expected to have a higher than usual incidence of cardiac anomalies and biliary tract cancer, establishing an associative link between these conditions.

In the study reported here, most of the cases were found to have extensive spread of cancer throughout the biliary tract and the liver, making the detection of biliary tract anomalies impossible. However, one case of intra-hepatic bile duct cancer with cardiac anomalies was noted in which tumor spread was not extensive, and non-uniform dilatation of intra-hepatic ducts was detected on microscopic examination of sections from the liver not involved by tumor.

As noted previously, a higher-than-expected incidence of multiple malignancies was seen in these cases of biliary cancer.[1,2] Of the 33 cases of bile duct cancer in this series, six had metachronous or synchronous second primaries (18%); in the background population the rate was only 6%, representing a statistically significant increase ($P \simeq 0.03$). Furthermore, the cases of bile duct cancer with congenital anomalies were 30% more likely to have second primaries than the ones without, although this difference was not statistically significant due to the small number involved. Several examples of agents that are teratogenic, mutagenic, carcinogenic, capable of producing congenital malformations, and capable of inducing cancer are known. It may be postulated that in utero exposure to such agents may have precipitated the development of cardiac anomalies, biliary tract anomalies, and ultimately carcinogenesis both in the biliary tract and at other sites throughout the body. This is, of course, strictly speculative, but it represents one possible intriguing explanation for the findings noted herein. More extensive studies are necessary, however, to delineate this syndrome.

Further research is needed since the findings discussed here were coincidental to the primary investigation, which was based on very small numbers. Certain biases in this type of data are possible. The methodologic problems in drawing conclusions from autopsy series were well recognized.[11] For example, selection bias may have occurred if the biliary tumor cases were sought out for autopsy because they were thought to have other interesting findings, such as unexplained heart disease. This, however, did not occur here since with all of these cases the heart disease was apparently asymptomatic and clinically unsuspected until the time of autopsy. Therefore, patients with bile duct cancer and cardiac anomalies were no more likely to undergo an autopsy than any other patients with bile duct cancer.

In situations such as these it is almost impossible to control all of the selection factors that determine autopsy.[11] At the institution studied here, autopsies are preferred for all patients who die. However, autopsy rates are low and have declined over time for complex reasons. Some information may be gained from looking at autopsy rates for the population of interest as compared to the whole autopsy population. From the tumor registry data for the series discussed, the recent autopsy rate for patients with bile duct cancer was estimated as 24%; the corresponding autopsy rate for all patients in the hospital was 19%. Thus the fact that the variables—age and sex distribution for cases and controls, the presence of cardiac disease and second malignancies for cases and controls, and the rates for autopsy for bile duct cancers and all cases—appear comparable provides some reassurance that the findings may point to a real association. Further reassurance may be achieved by comparing these cases not only to the overall population but to subgroups within this population.[11] For example, the incidence of cardiac anomalies in patients with bile duct cancer may be compared to the inci-

dence of cardiac anomalies in all cancer cases in the background population sample; the latter number is 2.9% and thus statistical significance is preserved. Nevertheless, the factors that may influence autopsy data associations are many and complex, and only a small part of the resulting bias may be measured or avoided.[11] Thus the conclusions drawn from this research must be viewed as tentative.

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Dr Widger's war

A photographic history of the 41st Portable Surgical Hospital 1943–1945

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In October 1942, Stanley W. Widger, a young surgeon who had recently opened a practice in Rochester, New York, began military training at Fort Devons, Massachusetts. Almost four years later, after serving in the South Pacific and Japan, he returned to his practice. Many American physicians had a similar experience although Stanley Widger may have been the only one who recorded the daily life of his unit in photographs.

The subjects of most of the photographs taken by Widger were the four medical officers and 32 enlisted men of the 41st Portable Surgical Hospital. The unit was organized in Oregon in the summer of 1943 and disbanded in Japan two years later. Widger photographed the men as they waited for and treated the casualties of World War II. He recorded scenes of what at first appears to be ordinary life—men bathing, using privies, posing for snapshots, setting up hospital tents, taking care of native children, and even building a sailboat. However, Widger also showed how the war intruded on this domesticity in photographs of surgery near the battlefield or of a dead Japanese soldier. The pictures that appear to be of ordinary life are in fact the most unusual ones since Widger's life in the 41st was rootless, improvised, full of uncertainty, and totally lacking in privacy.

The photographs taken by Widger are deceptively straightforward. The images will be familiar to anyone who has looked at family snapshot albums, magazine and newspaper photos, and the movie or television versions of M.A.S.H. (Mobile Army Surgical Hospital). Three New York newpapers that published several of Widger's photographs shortly after his death (*Democrat and Chronicle*, Rochester; *Standard*, Cortland; and *Newsday*, Long Island) presented them as striking pictures needing no further interpretation. The photographs are, however, complicated historical documents that may be better understood if placed in the context of their time.

Historians who study photographs know that contrary to common belief, the image does not mirror the reality. Photographs taken at different times, even in the recent past, were constructed using different norms of picture-taking. Such conventions influenced how a photographer created the setting for a picture and also what meanings could be derived from that picture. Conventions enabled a photographer to know, for example, how to array people and objects when possible, or how to frame them in his lens when unable to position them as he would like; where to stand in relation to his subjects; how much of what he saw to include in each photograph; and how much light was appropriate.[1-4]

Widger used three distinct sets of conventions in his photographs. The first and most familiar convention is that of the snapshot—the posed informal photograph intended to be a memento of a particular occasion. Photograph 1 is a snapshot taken of Widger as he was, he later wrote, "returning from (a) busy day in usual clothes" while the 41st was training in Medford, Oregon. The second set of conventions was that of the photojournalism of the 1930s and 1940s that told human interest stories. Photojournalists usually chose to limit the size of the space visible in the images in order to emphasize the subjects and meanings of their stories. The style of photojournalism is seen in the photograph depicting a corpsman "feeding an abandoned native baby . . . after things quieted down" on the island of Anguar in the South Pacific (Photo 2).

1. A snapshot of Dr Widger as he was "returning from (a) busy day in usual clothes" while training in Medford, Oregon.

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2. A corpsman "feeding an abandoned native baby . . . after things quieted down" on the island of Anguar.

The third set of photographic conventions used by Widger was that of medical and particularly of surgical photography. When he had a standard operating room, as he did in Japan in 1945 (Photo 3), Widger arrayed, lighted, and framed his subjects in ways that had become conventional by the 1940s. As this article will demonstrate, Widger adapted these conventions to the constraints of a portable surgical hospital.

Snapshots and photojournalism were familiar to most Americans in the early 1940s. The conventions of surgical photography were popular and photographs using these techniques were published in newspapers and magazines; photographs such as these were also used to build the stage sets for such successful movies as *Men in White*.[5] What is unusual is that an individual familiar with these visual languages used his camera frequently to record the daily lives of men who provided medical care during war.

There is some evidence available about how Widger learned the conventions of medical photography and photojournalism. During his residency he was interested in medical illustration and established a friendship with Nat Jacobs, an artist who sketched operations at Strong Memorial Hospital in Rochester, NY. Widger owned books by the photographers Alfred Steiglitz and Edward Steichen, and according to Mrs. Jane Widger "always enjoyed the photographs in *Life* magazine" (written communication, October 21, 1985).

3. Dr Widger operating in a standard operating room in Japan in 1945.

Widger made serious preparations for his war photography. His wife recalls that Widger bought a used Leica camera "as he was about to go overseas because he wanted a compact camera with a lens that was capable of extreme accuracy and sharpness." This camera had an interchangeable lens mount, and "it was flat, sturdy, and small enough so that it could be carried inconspicuously in his pocket." Just before he set out for the South Pacific from San Francisco, Widger arranged with the manager of a camera store "to have bulk 35mm film sent" to him on request.

Widger knew or suspected that he was unique in using the three sets of conventions to describe a medical unit during a war. In May 1983, shortly before his death, he wrote in outline form his "Recollections of World War II Service" and appended to it many of his photographs. This memoir, from which the quotes describing Photographs 1 and 2 are drawn, hints at some of the meanings Widger intended his photographs to convey. The memoir also suggests that Widger carefully chose those conventions appropriate for each photograph. For instance, he was precise about when and where he first encountered particular members of the 41st unit and identified them in each of the photographs appended to the memoir. "The boys," he wrote, "were loyal and were like a family."

As an officer, Widger chose an informal style of leadership; because he disliked military pomp and hierarchy, he preferred to be on a first name basis with the men he supervised. Moreover, he enjoyed the humor of incongruous situations. Thus the island of Anguar was "no place to come in by sailboat—as there was no wind and much shooting." His human interest photographs portrayed his detached humor and his beliefs concerning leadership.

Widger was a highly trained surgeon who had been chief resident at Strong Memorial Hospital. He was therefore dismayed when a professor of surgery at Stanford walked into his operating tent and said, "This man is in shock." Widger retorted "that I knew that," but later became friends with the physician and earned his respect by demonstrating skill at transfusing blood. Widger briefly summarized his surgical work in his memoir but concluded that the most important professional lesson he had learned during the war was that "a healthy young patient could stand practically anything, so one could 'get away with murder'. "

There are fewer surgical photographs in Widger's war memoir than there are snapshots and human interest pictures. Most of the surgical photographs were taken in Japan after he had left the 41st. Widger may have been too busy treating patients to take many photographs of surgical work under battlefield conditions. Those he took, however, conformed to the conventions of surgical photographs taken during the 1940s in permanent hospitals.

Many photographs were taken of the men of the 41st Portable Surgical Hospital. The photographs displayed here use the conventions of human interest photojournalism and medical photography rather than snapshots; these photographs are meant for personal use.

The photograph depicting a "Japanese soldier shot outside our sleeping tent" is striking since Widger rarely chose to photograph the painful experiences of combat. As he recalled later, during the landing on Anguar in Sep-

4. A "Japanese soldier shot outside our sleeping tent."

tember 1944 there was "much night anxiety, land crabs, shooting, and star shells with intermittent lighting up." It cannot be known precisely why Widger took so few photographs of men before, during, or after combat. Perhaps the best reason is that he had little time to do so because he was working hard, at least during and after combat. Moreover, as his son said in a newspaper interview shortly after his father's death, "I don't think he thought of himself as a photojournalist. I think he just took pictures that were indicative of his personality—sensitive and considerate. He considered photography a pleasant interlude in an otherwise unpleasant situation. (Vangorder G: War memories. *Standard,* Cortland, NY, July 26, 1984.)

The picture of the dead Japanese soldier depicts the intrusion of war into the familial world of the 41st after the "island was considered secured." This soldier, shot outside Widger's tent, was a personal rather than a generalized threat. The photograph evokes some of the clinical imagery that unlike conventional photographs of operating rooms, was withheld from the lay public. Mainly this photograph is a close-up human relations photograph. An additional message is suggested by the men walking in the left background. They ignore a familiar and macabre but no longer threatening scene.

In contrast, Photograph 5 seems bucolic and with its caption deliberately humorous. However, several other photographs taken by Widger present officers and enlisted men using outdoor privies while reading and talking with each other. These photographs are similar to a famous picture of Hungarian soldiers using an outdoor latrine taken during World War I by photographer Andre Ketersz.[6] Widger would not have known Ketersz' photograph, but he would have understood the story it told. Such photographs employ mundane imagery to depict the discontinuity between civilian and military life. There was much less privacy in the "family" of the 41st or any other military unit than in most civilian families. Human interest photographs such as these, that use familiar photographic conventions to depict a highly unusual subject, describe how men lived while they were in a war.

Photographs 6, 7, and 8 depict lighter moments during war; but they also may have had deeper meanings for Widger. All three are human interest close-up photographs. In Photograph 6, three men—two corpsmen of the 41st and a patient smoking a cigarette—appear to be smiling or laughing. During the more than a century during which medical photographs have been taken, many have depicted smiling patients. However, few of the patients were horizontal and none appeared to be on stretchers. Most readers have most likely already interpreted this photograph. This patient's participation in the war is over, if not completely at least for the time being. The men of the 41st are sharing this patient's good fortune. The cigarette, incidentally, reminds the viewer how the meaning of an image changes over time. To those of Widger's generation, a cigarette in a soldier's mouth was common; however, today it is a reminder that a cigarette was once a symbol of relaxation and normalcy among fighting men during war.

Photographs 7 and 8, like Photograph 2, were from a series of photographs taken by Widger on Anguar in September 1944. All three photographs depict enlisted men caring for native babies. The second photograph is a close-up of one man cradling a baby and looking into the distance away from the photographer. In Photograph 7 four men hold babies; one is bottle-feeding with a nipple made from the finger of a surgical glove. Finally, in Photograph 8 a shirtless corpsmen and a baby sit behind a sign advertising the 41st Portable Surgical Hospital.

Like the photographs of the latrines, these pictures are similar to photographs taken by other photographers. Dr Christopher Lawrence of the Wellcome Institute for the

5. "Latrine—no privacy but what a view."

6. Two corpsmen and a patient of the 41st.

7. Four corpsmen caring for native babies.

9. A photograph of one of Dr Widger's medical colleagues in an empty operating theater.

History of Medicine in London found an official photograph of British soldiers in Sicily in 1943 weighing a baby. Lawrence interpreted this photograph as showing nostalgia for home and perhaps suggesting the civility of British soldiers, who were willing to pause in the midst of war to nurture an infant. Widger's photographs may have been intended to convey similar meanings.

Widger may have intended his pictures of men with infants to convey a different meaning than the official British photograph. In the society of men at war, unlike civilian life, men are required to play nurturing roles; to comfort by word and touch and to nurse. They may sometimes be uneasy about these culturally unfamiliar roles. The babies pictured here may have offered the enlisted men who held them—none of the photographs depict physicians holding babies—a way to express pride in their ability to nurture in a way totally acceptable by civilian society. Photograph 7 emphasizes that for the 41st, nurturing was a collective activity. Photograph 8, however, is more revealing. The placement of the sign identifying the 41st suggests that perhaps Widger intended the photograph to be used as a souvenir. He did not choose to put the sign in front of what must have been a more frequent scene—an enlisted man nursing a wounded soldier.

This interpretation is at the boundary of permissible historial analysis. It is deduced from conventions of style and subject matter and from knowledge of American social history. Photographs of women nurses with babies were taken in clinics and hospitals during the first half of the 20th century. Widger is unique in that he photographed males using conventions usually applied to women. By taking at least a dozen photographs of enlisted men with native babies, Widger signals that although the event was unusual, the meaning was important to him and perhaps to other members of the 41st. At the very least, something made these images "cute" or "engaging" when Widger saw them and picked up his camera to frame them. However, it cannot be known precisely what motivated Widger to take these photographs.

The final three photographs depict the ways in which Widger adapted medical photographic conventions to the unique working conditions of a portable surgical hospital. In Photograph 9 the conventions of the snapshot were combined with medical photography by including one of Widger's medical colleagues. In another photograph of the same scene, only the medical photographic convention was used. In this photograph, the operating theater is viewed from the entrance. Above the table hangs a surgical lamp; beneath and behind it are various receptacles. Above the lamp a light-colored cloth marks the area in

8. A corpsman and baby sitting behind a sign advertising the 41st Portable Surgical Hospital.

10. Two surgeons preparing equipment for administering anesthesia.

11. Dr Widger performing surgery while on the island of Anguar.

which the surgical team will work. To the rear are the walls of the tent and beyond the tent to the right is the outdoors. The men of the 41st had created a medical setting that Widger photographed in the conventional manner.

In Photograph 10 two surgeons prepare to work in the same operating room. The physicians are depicted preparing the equipment used to administer anesthesia. As in most civilian photographs of anesthesia preparation taken in the 1940s, the equipment is in the foreground and the men beside and behind it. Because of the tropical climate, however, bare torsos have replaced surgical gowns.

The final photograph depicts Dr Widger operating while on the island of Anguar. He is capped, gowned, and masked despite the heat. The surgeon, unlike the anesthetist at this operation, could not deviate from the rules of scientific medicine without endangering the life of the patient. The photograph is conventional, except that the space is more compressed than in most pictures taken of surgery in the 1940s. As noted with the photographs of the operating theater and of the anesthetists preparing their equipment, the viewer must first imagine how the photograph would have looked if it had been taken in a standard hospital. The photographer would have been placed slightly above and to one side of the surgeons, perhaps looking down from an amphitheater. The photograph would have been framed with the walls of the theater and the bodies of the surgeons and spectators. This is what Widger may have instructed the individual who took the photograph to do here. The result is striking: a conventional photograph of surgery in an unusual setting.

Stanley W. Widger was a historian of an important episode in modern military medicine. He produced what may be the first thoroughly documented account of the application of the science and technology of surgery in a portable field hospital in World War II. His story is unusual because it was told in photographs and because he used the conventions of the snapshot, photojournalism, and medical photographs to depict the men of the 41st Portable Surgical Hospital.

Acknowledgments. The author thanks Mrs Jane Widger for sensing the importance of the photographs and making them available for study. The quotations and photographs in this paper appear with the permission of Mrs Widger, and remain in her possession. The author is also grateful to Stanley Widger for taking and, in the final months of his life, printing and annotating many of the photographs.

Note. A reviewer of this paper for the *New York State Journal of Medicine* questioned whether personal photography was permitted in combat areas. Staff of both the Military Archives and the Library and Printed Archives Branches of the National Archives can find no pertinent regulation prior to 1949. Published sources, however, confirm that regardless of the regulations, personal photographs were frequently taken. For example, in *The Camera at War* (New York, Simon and Schuster, 1978, p 95), Jorge Lewinski wrote " . . . there was an undetermined number of amateur photographers [who included] the soldiers in possession of a camera. During the later stages of the war in Europe, practically every second Allied soldier managed to get hold of a camera." From a British perspective, the Labour Party leader, Dennis Healey, recalls that "in landing on Sicily I dropped my camera on the beach . . . it was never the same again." (*Healey's Eye: A Photographic Memoir*, London, Jonathon Cape, 1980, p 18–19.) Mrs Widger recalls that Dr Widger's film was sent to his half-brother in Syracuse either during the war or the occupation of Japan and thus was available to the military censors.

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The child with short stature

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A child with short stature may be the cause of anxiety and emotional concern for his or her family. Further, many short children suffer significant physical and social embarrassment because of their stature. At the Human Growth Hormone symposium held in Baltimore in 1983, it was suggested that there are currently 1.8 million children who will attain adult statures of less than the third percentile. It was also stated that as many as 24,000 children would benefit from growth hormone (GH) therapy. Until recently the only children eligible for treatment with GH were those with a deficiency (failure of an adequate response of GH to standard pharmacologic testing). This concept is presently being reevaluated since there is increasing evidence that an adequate response of GH to pharmacologic testing may not define the actual neurosecretory dynamics of GH release in an individual. Indeed, children with normal GH response to standard pharmacologic tests may benefit from treatment with GH.

The following review includes a brief summary of normal growth, a study of the recent advances in the diagnosis and treatment of a child with short stature, and serves to acquaint the reader with the current controversy of the role of GH therapy in the short child.

GROWTH DEFINITIONS

Human growth is characterized by rapid fetal growth, a deceleration of growth rate following birth, a period of relatively slow but continued growth during childhood, a rapid growth spurt during puberty followed by a gradual deceleration, and finally a total cessation of growth with epiphyseal fusion.[1] During fetal life intrauterine growth is modulated by placental function, maternal size and nutrition, and maternal health. Further, exogenous agents such as ethanol and nicotine may alter growth. Size at birth appears to be related more to maternal size than to genetic factors.[2] Peak intrauterine growth velocity occurs at approximately the fourth month of gestation.[3] Hormonal factors regulating fetal growth include insulin and thyroid hormone. The contribution of somatomedins (low molecular weight peptide growth factors) to fetal growth is less clear; recent evidence has shown that somatomedin-C levels are very low at birth and in the neonate.[4]

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The male fetus grows faster than the female, predominantly after 32 weeks' gestation.[5] The growth of the male infant for the first three to six months after birth is also slightly faster than that of the female. The early acceleration of male growth may be due to the initial transient increase in testosterone secretion in male newborn infants.[6] Thereafter there is no sex difference in growth rate until adolescence.

The shifting of linear growth percentiles during the first two years of life is frequent and normal, as intrauterine factors lose and genetic factors gain importance in growth.[7] After two years of age, there is a tendency for each child to follow a consistent growth percentile. It has been demonstrated in children with a delay in growth and development that an exaggerated regression to the lower percentile channels may occur over the first five years of life.[8] It is important to recognize this entity as a normal variant of early childhood growth. In most other instances, however, deviations from a child's previous growth percentiles may indicate a pathologic process. After the first two years of life, until puberty, the average growth rate is 6.25 cm/yr with a range of 4 to 7.5 cm/yr. Growth rates of less than 4 cm/yr are abnormal. During puberty marked increments in growth velocities occur: in girls the range of pubertal growth is 14 to 25 cm, and in boys the range is 15 to 38 cm.[9] The peak yearly pubertal growth rate for girls is 8.3 cm (6.2 to 10.4) and for boys is 9.4 cm (7.2 to 11.8).[10]

Normal growth. Normal growth is dependent on a number of factors, including adequate nutrition, a stable emotional environment, the absence of chronic illness, and the interaction of numerous hormones. The major hormones that affect growth are GH, thyroxine (T_4), sex steroids, Vitamin D and parathyroid hormones, and corticosteroids. Most investigators agree that the skeletal growth-promoting actions of GH are mediated through the somatomedins.[11] However, there are controversial data that GH may also act directly to stimulate cartilage and long bone growth.[12] The release of GH is regulated by the interaction of two hypothalamic hormones: growth hormone releasing factor (GRF) and growth hormone release inhibiting factor, or somatostatin (SRIF). GRF was initially isolated from a human pancreatic tumor cell line[13,14] and has most recently been isolated from cerebral spinal fluid.[15] Both the 40 and 44 amino acid forms have been isolated from the hypothalamus.[16]

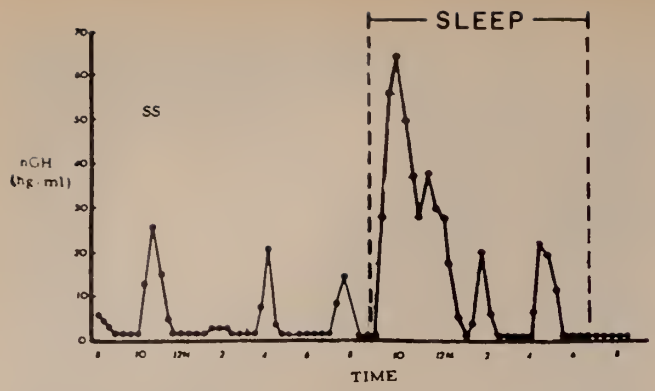

FIGURE 1. Growth hormone secretory pattern in a child at puberty. The sleep period is enclosed in dashed lines. (Reproduced from [20] with permission.)

The administration of synthetic GRF causes the release of GH.[17] GRF exerts its action via cyclic adenosine monophosphate (AMP) to mediate the release of GH[18]; SRIF inhibits GH release. The release of GH has been further demonstrated to be inhibited by somatomedin, which may also stimulate SRIF release.[19]

Growth hormone is released in pulses throughout the day with the frequency of pulsatile secretion increasing during the sleep periods (Fig 1).[20] There are approximately seven to eight pulses of GH during a 24-hour period.[21] The release of the hormone during the sleep periods appears to involve stimulation of serotonin receptors; GH release is enhanced during adrenergic and dopaminergic stimulation.[22]

Abnormal growth. A child is considered short if his or her standing height is two standard deviations or more below the mean for his or her age (less than the third percentile on a normal growth curve). Poor growth is considered a growth rate of less than 4 cm/yr after the first two years of life and prior to puberty.

The establishment of a child's growth rate is the first step in evaluating a child with short stature. Growth curves are available for American children[23] and for midparent adjusted height corrections.[24] Poor growth rates are defined for various ages by the 1983 criteria of the National Hormone and Pituitary Program: 0 to 1 year, <11.0 cm/yr; 1 to 2 years, <7.0 cm/yr; 2 to 3 years, <5.0 cm/yr; 4 years to puberty, <4.5 cm/yr; and pubertal years, <5.5 cm/yr.

Body proportions are also important in evaluating abnormal growth rates.[11] The upper to lower segment ratio (head to pubis/pubis to heel) is one common measurement. At birth this ratio is approximately 1.7 and decreases progressively; by adulthood it is close to 1.0. In adult black individuals the upper/lower segment ratio is close to .85 to .90.[25] It is often helpful to define height and weight as height age or weight age. This method was first used by Wilkins to represent the age at which a child's height or weight would fall at the 50th percentile. In children with hypothyroidism or growth hormone deficiency, for example, both the height age and weight age are less than the chronologic age. However, the height age is often more delayed than the weight age, giving the child an obese appearance.

A bone age radiograph of the hemiskeleton, knees, or hands and wrists is used to establish an index of physiologic age or maturation.[26,27] When an organic cause is responsible for an abnormality in linear growth rate, a delay in the physiologic maturation index or bone age may exist.

The initial laboratory examination of a child with a height less than the third percentile and a deficient growth rate should include a complete blood count with differential, biochemical profile, and sedimentation rate as well as a urine analysis. These tests aid in determining whether a systemic illness exists. Laboratory testing should also include thyroxine and thyrotropin or thyroid stimulating hormone (TSH) levels to evaluate thyroid gland function. In girls with short stature a banded karyotype of the peripheral lymphocytes should be considered to examine the possibility of gonadal dysgenesis (eg, 45X or mosaicism of the X chromosome). Specialized endocrine tests should not be initiated in children with short stature or poor growth until chronic disease or abnormality of thyroid function have been excluded. At such time a lateral skull radiograph should be considered to evaluate the pituitary region.

Screening tests for the secretion of GH include post-exercise or sleep sampling.[28] Since the late 1970s radioimmunoassay of somatomedin-C (SM-C) has been used to screen for biologic activity of GH.[29] The somatomedins are a family of low molecular weight peptides produced predominantly in the liver and SM-C has been considered the mediator of GH activity.[30] In the past a low SM-C level was thought to be associated with decreased GH activity and a normal SM-C with normal GH secretion. It has now been demonstrated, however, that this correlation is not always present.[31,32] A child may grow at a normal rate and yet have low SM-C levels. Thus the measurement of SM-C may not be as useful as previously suggested.

Definitive tests for the secretion of GH include provocative tests with a number of pharmacologic agents[33]: arginine, 0.5 g/kg of body weight over 30 minutes by intravenous infusion; insulin induced hypoglycemia, 0.1 U/kg by rapid intravenous infusion; L-dopa, 250 mg orally if less than 30 kg body weight and 500 mg orally if greater than 30 kg body weight; and glucagon, 0.1 mg/kg intramuscularly, maximum 1 mg). Two tests are often used sequentially or together since the response to any one agent has only an 80% reliability; this is increased to greater than 90% with a double stimulation test.[33] It has been suggested that adolescents should be primed with oral androgens or estrogens for three to seven days prior to testing in order to differentiate GH deficiency from an inadequate GH response. An inadequate hormonal response is often associated with a delay in growth and pubertal development.[34] In the past a GH response of greater than 7 ng/mL to a provocative test was considered adequate growth hormone reserve. Therefore such patients had not been considered candidates for growth hormone therapy.

Genetic Short Stature and Constitutional Delay

Two conditions exist in which a child's height is less than or equal to the third percentile for age but the growth rate prior to puberty is often in the low normal range. In the first condition—genetic short stature—the children

are usually from short families. In such a situation, bone age is normal for chronologic age, and a short adult height is eventually achieved. A second cause of short stature is constitutional delay in growth and pubertal development. In this case there is often a family history of late development. Although bone age is less than the chronologic age, children with this condition may be expected to undergo a normal puberty at a later age than average and usually achieve a normal adult stature.[1] These two conditions, genetic short stature and constitutional delay in growth and development, are the most common forms of short stature in childhood today.

These two conditions have recently been subject to intensive clinical investigation. Currently there are ongoing trials to evaluate whether the administration of growth hormone to children with genetic short stature or constitutional delay in growth and pubertal development will increase their ultimate adult height.[35] In the late 1970s Kowarski and associates[36] described two children who had growth failure with low somatomedin activity and normal GH response to stimulation. Treatment with exogenous GH resulted in both an increment in SM-C levels and an improvement in growth velocity. Rudman and coworkers[37] subsequently reported on nine children with poor growth rates, very low somatomedin levels, and normal GH levels on radioimmunoassay, but who had low GH levels on bioassay. These children were treated with GH and demonstrated improved growth rates comparable to those noted in GH-deficient children who are treated with growth hormone. Rudman suggested that his patients had biologically inactive GH levels that resulted in their deficient pretreatment growth rates. It has been suggested that Rudman's patients represent a very select group of children since the growth rates were significantly lower than those often noted in children with hypopituitary dwarfism.[35]

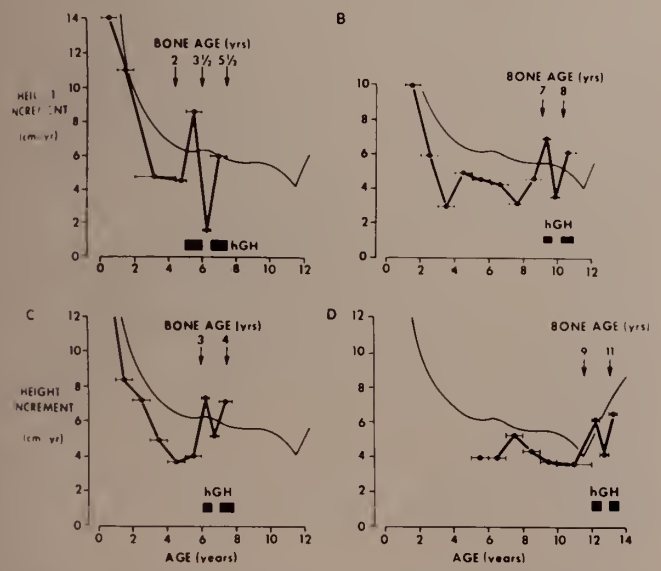

FIGURE 2. Effect of reinstitution of growth hormone therapy (**heavy lines**) on growth rates in four children with normal immunoreactive growth hormone secretion in whom an increase in growth rate had occurred during a six-month trial of growth hormone. (Reproduced from [35] with permission.)

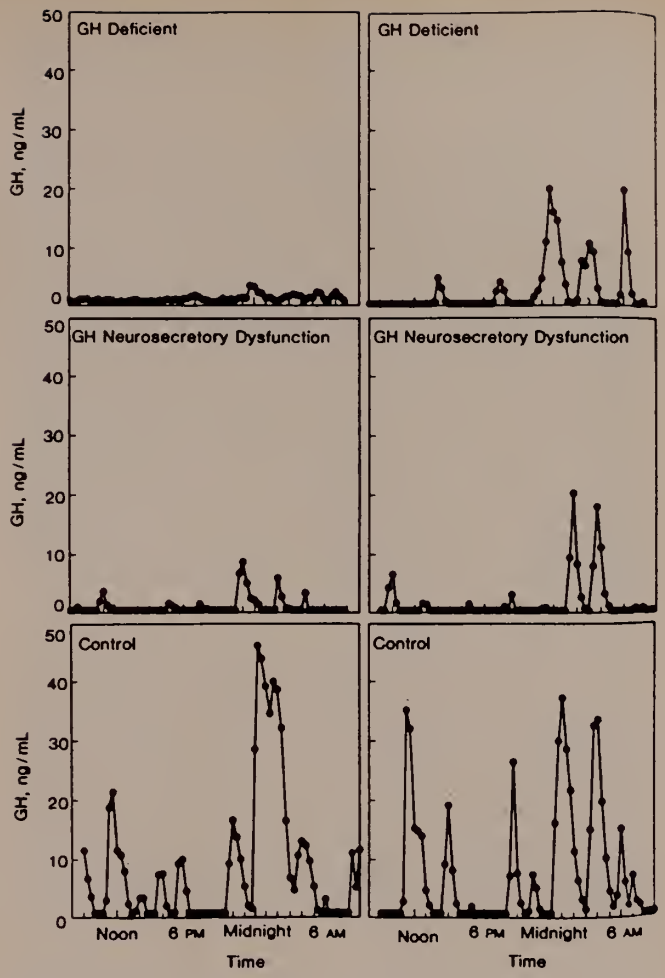

FIGURE 3. Representative 24-hour GH secretory patterns in GH deficient children, those with GH neurosecretory dysfunction and controls. Patients with GH deficiency and GH neurosecretory dysfunction are in Tanner I. Lower left control is in Tanner I and lower right is in Tanner V stage of puberty. (Reproduced from [39] with permission.)

A group of children with short stature who had normal GH responses to standard provocative testing was reported on by Van Vliet and colleagues.[35] This group initially studied 15 children, 4 to 15 years of age, who had low normal somatomedin levels and who were growing at less than 5 cm/yr despite normal GH responses to provocative testing. Of these children, six treated with GH had marked increments in their growth velocities. These children were the younger of the tested group and had the most delay in their bone ages (Fig 2).

The secretory dynamics of GH in normal short children was further studied by Bierich[38]; integrated serum GH levels were evaluated at all levels of puberty as compared to matched controls. He concluded that treatment with exogenous GH was warranted in children with constitutional delay in growth and development. Spiliotis and coworkers[39] also evaluated the neurosecretory dynamics of GH in normal short children who were growing at less than the third percentile and who had normal GH responses to provocative testing. In this study the measurement of growth hormone—every 20 minutes for 24 hours—revealed both a decrease in the number and the amplitude of spontaneous pulses of GH (Fig 3). The patients

also responded with improved growth velocity when given GH therapy. Similar results were reported in a small group of normal short children treated by Gertner and associates.[40]

Some normal short children may respond with improved growth rates to treatment with exogenous GH. It may well be that children with genetic short stature or constitutional delay in growth and development may have a degree of neurosecretory dysfunction with respect to GH secretion or reserve. It is now apparent that this dysfunction may only be observed if multiple blood sampling for GH is obtained throughout the day, since normal GH response to provocative testing may not correlate with the growth velocity and GH secretory pattern. It is important to carefully evaluate the growth rates of these children prior to and during GH therapy so that data may be generated with respect to the increment in growth velocity in these populations. With the prospect of an unlimited supply of GH synthesized by recombinant DNA techniques, less restricted treatment of short children with GH may be anticipated.[41,42]

Causes of Abnormal Growth

The causes of short stature may be divided into primary and secondary groups (Table). Primary growth deficiency is most often expressed prenatally and is due mainly to defects of skeletal growth or to major genetic abnormalities. Secondary growth deficiency expressed prior to birth is usually caused by maternal factors such as poor maternal nutrition, alcohol ingestion, maternal infection, or maternal hypertension during pregnancy. Many of these children will grow normally after birth.

Secondary growth deficiencies that occur after birth deserve careful evaluation because once the cause is identified, specific treatment may correct most of these problems and allow for a return of normal growth. These conditions include nutritional deficiency, emotional deprivation syndromes, chronic illness, or specific hormonal deficiencies such as thyroid or GH deficiency.

Recently Schaff-Blass and colleagues[43] offered similar categories for characterizing growth disorders in children. Intrinsic shortness is a situation in which children are destined to become short adults. These children usually have normal growth velocities, and they grow parallel to but below the third percentile; their bone age approximates their chronologic age. Delayed growth manifests as a delayed puberty and a bone age approximately equal to the height age. These children should eventually obtain a normal adult height. Attenuated growth is a situation in which an underlying abnormality usually exists. These children have abnormal growth rates and bone age may be delayed. Unless the condition is reversed or treated, these children may experience severe growth retardation.

Uncommon Forms of Abnormal Growth

A number of uncommon forms of abnormal growth have recently been reviewed in the literature.[44] The following are conditions associated with abnormal growth that are perhaps not widely appreciated, and in which a high index of suspicion is often needed to establish the correct diagnosis.

Psychosocial dwarfism. A group of children with severe linear growth retardation associated with abnormal and bizarre eating patterns, an abnormal parent-caretaker/

TABLE. Causes of Short Stature

Features	Primary skeletal growth deficiency	Secondary growth deficiency: Prenatal onset	Secondary growth deficiency: Postnatal onset
Onset of growth deficiency	Usually prenatal	—	—
Rate of maturation	Variable, usually normal	Variable, slow to normal	Usually slow
Malproportion	Frequent	Variable	Unusual, except in rickets
Associated anomalies	Frequent	Variable	Unusual, except causative anomaly
General causes	Chromosomal abnormalities	Crowding (eg, twins)	Nutritional deficiency, neglect, poor absorption
	Mutant gene disorders, including osteochondrodysplasias	Maternal:	Mental deficiency
	Syndromes of unknown cause	Small mother	Cardiac defect
		Low socioeconomic status	Renal dysfunction
		Malnutrition	Respiratory insufficiency
		Hypertension	Growth hormone deficiency
		Toxemia	Thyroid hormone deficiency
		Renal disease	Still's disease
		Heart disease	Metabolic disorders
		Cigarette smoking	
		Heroin addiction	
		Ethanol intake	
		Hydantoin therapy	
		Warfarin therapy	
		Rubella	
		Cytomegalic inclusion disease	
		Toxoplasmosis	
		Syphilis	
Therapy to increase eventual stature	None to date	May or may not show postnatal catch-up growth	Specific treatment yields catch-up growth

From Smith.[1]

child relationship, and abnormalities in endocrine function was described by Powell and associates.[45,46] These children often present with abnormal eating (polyphagia, gorging, and vomiting) and drinking (polydipsia) habits and other behavioral abnormalities. The most complete recent review of this condition suggested that psychosocial dwarfism is due to an inhibition of hypothalamic releasing factors that is both intermittent and reversible in nature.[47] Confirmation of the diagnosis of psychosocial dwarfism is made when linear growth quickly returns to normal when the child is removed from the home environment.

Feeding disorders. Patients with anorexia nervosa have been found to have decreased linear growth despite the presence of GH levels responsive to stimulation.[48] Reduced levels of somatomedin, presumably secondary to the severe state of malnutrition, have been suggested as the cause of this growth failure.[49] Recently, researchers described a more subtle form of feeding disorder in which poor linear growth was observed.[50] In their cases patients 9 to 17 years of age had self-imposed restricted caloric intake. The mean weight deficiency for height was 10.1 ± 6.6% and was subtle in many cases. A weight gain occurred prior to the acceleration of linear height velocity in this study. Thus in our society in which thinness is viewed as a positive attribute, careful attention must be paid to a child's caloric consumption. In an effort to conform to a family's dietary pattern a child may seriously self-restrict his or her intake or be restricted by an adult from receiving an appropriate caloric intake for age.

Growth failure after cranial irradiation. Deficient growth rates in children who have received irradiation of the central nervous system for malignancies have been noted recently in the literature.[51,52] Many of these children have normal GH responses to provocative pharmacologic stimulation tests.[51] Chrousos[53] reported that monkeys who had received central nervous system irradiation had decreased and deficient amplitude of GH pulses as measured during a 24-hour period when compared to control animals. Subsequently, Blatt and associates[54] reported abnormal GH pulses in children who had received sanctuary irradiation for acute lymphoblastic leukemia. The efficacy of GH in children with abnormal growth rates but with normal GH response to provocative testing was reported by Romshe and colleagues.[52] Although the increment in growth velocity was not as great as that observed during hormonal therapy of children with low GH levels, the reported growth rates tripled from their pretreatment velocities. In another study, the use of GRF was evaluated in children suspected of having a neurosecretory defect in GH release.[55] In these patients abnormal responses of GH to provocative testing but released GH in response to GRF stimulation was common. GRF aided in determining the hypothalamus as the site of the abnormality of GH release. At present, only treatment with GH may be offered to those children. In the future, however, a trial of GRF may be helpful in children with a hypothalamic defect in the neuroregulation of GH release.

Treatment of Short Stature

Human cadaver growth hormone. Successful treatment of GH deficiency with human cadaver growth hormone was reported in 1958[56] and since that time more than 27,000 GH-deficient children have been treated. More than 25 years of experience with GH therapy was recently reviewed by Frasier.[57] Until recently cadaver growth hormone has been provided by the National Hormone and Pituitary Program (NHPP) to children defined as deficient by their GH responses to stimulation. Cadaver growth hormone has been supplied at no cost, provided the child was enrolled in an approved clinical research protocol or had spontaneous hypoglycemia. The recommended dose of cadaver growth hormone, 0.06 to 0.10 U/kg three times a week intramuscularly or subcutaneously, required approximately 30 to 50 cadaver pituitary glands per child for one year of GH treatment. Treatment was provided by the NHPP until a height of 163 cm (50th percentile) for a girl or 168 cm (10th percentile) for a boy was achieved. Therapy was not routinely approved when the child's bone age was greater than 14 years. Human cadaver growth hormone has also been available from commercial drug companies at a cost of approximately $10,000 per year.

Recently, death from a degenerative neurologic disease was reported in three young men 3, 10, and 16 years after cessation of treatment with NHPP growth hormone.[58] These young men had been treated for five to 12 years between 1963 and 1980. Autopsy performed on two of these patients demonstrated findings consistent with Creutzfeldt-Jakob disease (CJD). A fourth patient, a woman, has recently been reported as also having CJD.[59] This disease is one of a family of subacute spongiform encephalopathies caused by a slow virus. The exact nature of the infectious agent causing CJD is not known. It is postulated that one or more lots of cadaver growth hormone distributed by the NHPP may have been contaminated with the CJD pathogen.[58] The NHPP has suspended its distribution of human cadaver growth hormone until animal studies determine if transmission of CJD occurs following GH injection. It is anticipated that these studies will take one and one half to three years to complete. Additionally, the distribution of commercial supplies of cadaver growth hormone in the United States has been suspended.

Synthetic growth hormone. In 1982 clinical trials of synthetic GH were initiated. Biosynthetic methionyl growth hormone is produced through genetic engineering or recombinant DNA techniques. A partly synthesized human growth hormone gene is inserted into a plasmid

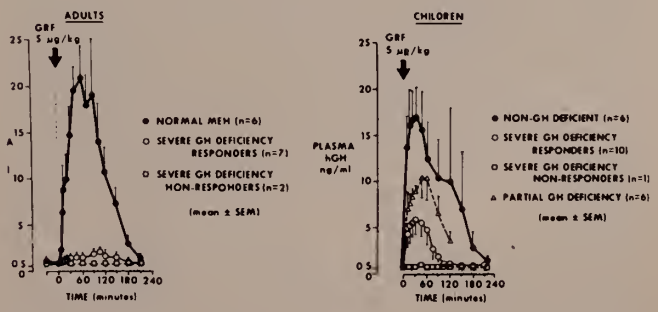

FIGURE 4. Effect of GRH-44 (5 µg/kg) on mean concentration of plasma GH (±SEM) in normal young adults and GHD adults (**left panel**) and non-growth hormone deficient and growth hormone deficient children (**right panel**). (Reproduced from [17] with permission.)

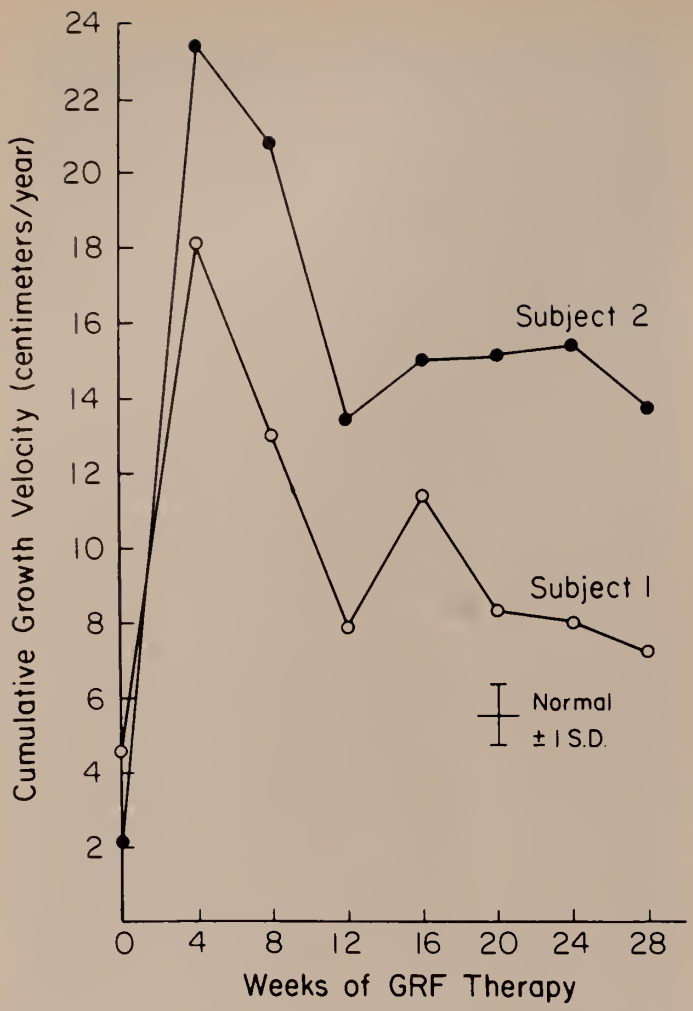

FIGURE 5. Cumulative linear growth rate determined at four week intervals before and during six months of GRF therapy. (Reproduced from [66] with permission.)

and then expressed in the *Escherichia coli* bacteria. The synthesized growth hormone is identical to human cadaver growth hormone except for the addition of the N-terminal methionyl group. Methionyl growth hormone (Met-GH) and human cadaver growth hormone are equally effective in their ability to bind to the human growth hormone receptor site.[41,42] The changes in somatomedin, blood urea nitrogen, triglycerides, and oral glucose tolerance in response to met-GH administration are identical to those following the administration of human growth hormone. Changes in linear growth have been reported to be comparable as well.[42] Greater than 125 children have received met-GH under research protocols in 24 institutions in the United States (personal communication, S. Kaplan). The longest period of treatment has been approximately three years and no significant reactions have been reported.

Since the distribution of human cadaver growth hormone in the United States was discontinued, the Food and Drug Administration has approved treatment with met-GH for children with growth hormone deficiency. Currently trials are underway with other preparations of synthetic GH. It is anticipated that synthetic GH will become a less expensive alternative for GH therapy than commercially obtained human cadaver growth hormone.

Growth hormone releasing factors. The newest agent available for the evaluation and possible treatment of growth disorders is growth hormone releasing factor (GRF). Initially isolated and sequenced from a pancreatic tumor cell line (hpGRF),[13,14] GRF was subsequently isolated from hypothalami of several species.[16] The tumor line GRF and human hypothalamic GRF have an identical primary structure and are identical in activity.[16] GRF has been infused in both normal children and adults (Fig 4)[17,60–64] and the GH that is released has been identified to be preformed growth hormone.[16] The major side effect of single dose GRF administration is brief flushing after initial infusion in fewer than 5% of the patients.[63]

In a recent report by Thorner and co-workers[65] the use of GRF resulted in the acceleration of linear growth in two GH-deficient children (Fig 5). In this instance the biologic effects of GRF included an increase in nitrogen retention and somatomedin. At the present time GRF has been administered in a nasal preparation with no untoward effects under experimental conditions.[66] It has been speculated that this nasal preparation may become the future route of administration of GRF and indeed in cases of hypothalamic growth failure, GRF therapy may possibly replace GH treatment in the future.

Androgen therapy. Anabolic steroids have been used for the treatment of short stature caused by constitutional delay in maturation in cases where the delay in maturation in boys has caused significant social discomfort. Rosenfeld[67] reported that intramuscular injections of testosterone at doses of 200 mg/mo for three to four months resulted in the appearance of secondary sex characteristics accompanied or followed by an increment in growth velocity. This treatment did not cause rapid epiphyseal closure or suppression of subsequent spontaneous pubertal development. Rosenfeld recommended that young men treated in this manner should have a minimum age of 14 years with a serum testosterone level of less than 100 ng/dL.

Summary

During the past five years, the definition of normal growth hormone reserve has become increasingly less clear. It is known that a normal hormonal response to stimulation may not accurately define GH reserve. It is apparent that various altered growth patterns may represent subtle forms of neurosecretory disturbances in GH release. Indeed, patients who were previously thought not to benefit from growth hormone therapy, such as those with genetic short stature or constitutional delay in growth and development may profit from such treatment. The availability of synthetic growth hormone offers the prospect of an unlimited supply of the hormone. Growth hormone releasing factor provides a new method of evaluating the short child and may provide a specific mode of therapy for the child with neurosecretory dysfunction of GH.

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Campylobacter infection mimicking ulcerative colitis

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In the past ten years, as a result of new stool culture techniques, *Campylobacter jejuni* (also known as *Campylobacter fetus* ss *jejuni*) has become recognized as a significant cause of bacterial diarrheal disease in man. Although this is not a new pathogen, it has only recently been associated with this clinical presentation.[1]

Infection caused by *Campylobacter jejuni* typically presents as an acute diarrheal illness with abdominal cramping, nausea, and fever. The diarrhea is usually watery but may frequently become bloody; leukocytes are generally present.[1-3] The abdominal pain may be severe and associated with tenderness, particularly in the lower abdomen. The patient may also appear acutely ill.[2]

Although detailed studies of patients with campylobacter infection are not available, it has generally been thought that the disease affects the jejunum and ileum.[4] In the past several years, reports of campylobacter infection with colorectal involvement have emerged with cases presenting as primarily colitis.[3,5,6] The following is a report of a case of *Campylobacter jejuni* colitis similar in both clinical and anatomic presentation to new onset ulcerative colitis.

CASE REPORT

A 23-year-old Jewish medical student came to the emergency room complaining of abdominal cramps, headache, diarrhea, and hyperventilation for one day. He had been anxiously preparing for the National Board examinations that he was scheduled to take two days later. The patient had been in good health with no chronic abdominal disorders. He could not recall eating any unusual food, but he had eaten at various neighborhood restaurants recently. The patient denied any traveling, household pets, homosexuality, or inflammatory bowel disease.

On examination the patient appeared anxious and uncomfortable; he had a fever of 101.6°F orally. There was voluntary guarding and mild tenderness on deep palpation in the lower quadrants of the abdomen. On digital examination rectal tenderness was noted. Examination of the stool revealed a liquid, yellow-brown, strongly guaiac positive specimen that was filled with polymorphonuclear leukocytes and, to a lesser extent, red blood cells on microscopic study. Complete blood cell count revealed a peripheral white blood cell count of 8,800/μL and a hemoglobin of 15 g/dL. Abdominal radiograph showed a nonspecific gas pattern.

A rigid sigmoidoscopic examination performed to 18 cm revealed 3+ erythema, granulation, friability, and a loss of the normal vascular pattern from rectum to sigmoid. Discrete ulcers were not seen. A rectal biopsy and stool cultures were taken.

At that time the patient was thought to have acute proctosigmoiditis due to either a bacterial pathogen or new onset ulcerative colitis. Because of the serious consideration of a possible *Shigella* infection, he was given ampicillin orally.

Examination of the rectal biopsy (Figs 1,2) showed mucosal ulceration, acute inflammation, crypt abscess formation, and goblet cell loss. No granulomas or amebae were seen. Gram stain revealed no organisms within the bowel wall. Bacterial culture of the stool, however, revealed *Campylobacter fetus* ss *jejuni* four days later.

By this time the patient had improved markedly; the fever had abated and the diarrhea resolved. Small amounts of loperamide hydrochloride had been cautiously used on the third and fourth days of the patient's illness to allow him to take his board examinations, but was then discontinued. The patient continued to do well; antibiotics were stopped and he was totally asymptomatic after one week. Repeat sigmoidoscopic exami-

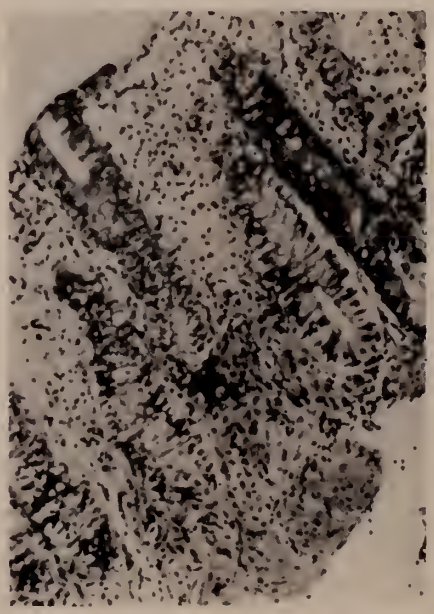

FIGURE 1. Rectal biopsy showing active colitis with mucosal ulceration, colonic inflammation, and goblet cell depletion. (hematoxylin and eosin stain; original magnification X 100)

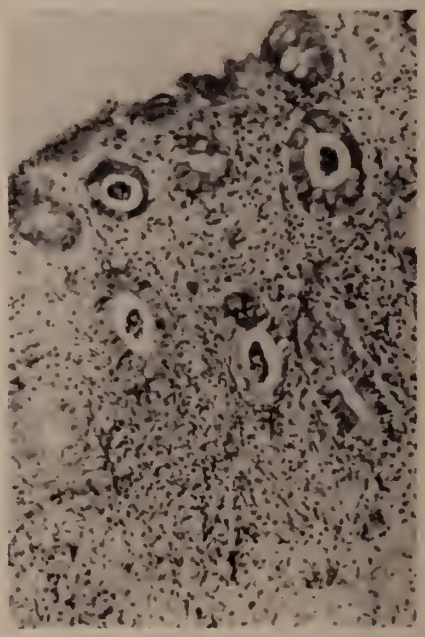

FIGURE 2. Another field of same rectal biopsy sample showing crypt abscesses. (hematoxylin and eosin stain; original magnification X 100)

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nation two weeks later showed normal mucosa and vascular pattern. The patient has remained well since.

Discussion

In this case of colitis caused by campylobacter infection, without bacteriologic data this patient's illness could easily have been confused with ulcerative colitis at initial presentation. The patient, a young Jewish man under acute psychologic stress, had bloody diarrhea and a rectal biopsy compatible with ulcerative colitis showing mucosal ulceration, acute inflammatory changes, goblet cell loss, and crypt abscesses. The critical point, however, is that these findings are nonspecific and may be seen not only in ulcerative colitis, but also with other infectious agents such as *Shigella*, *Salmonella*, amebae, and *Neisseria gonorrhoeae*.[7]

One feature of infectious colitis that may help to distinguish it from true ulcerative colitis is that in most varieties of infectious colitis, as in this case, there is preservation of glandular architecture as opposed to distorted crypts and glands.[7] Crypt atrophy and the presence of a villous-like surface appearance—caused by the separation of crypts—are additional histologic features that help distinguish ulcerative colitis from acute, self-limited colitis.[8] Actual culture, of course, remains the definitive standard for diagnosing an infectious colitis. Special culture techniques and selective media and microaerophilic conditions are required to grow *Campylobacter*, but this is easily and routinely done by most clinical labs, if desired.[1,2]

The frequency of campylobacter infection in diarrheal illness is surprisingly high. Studies have estimated the incidence of campylobacter infection to be 5% to 11% of all acute diarrheal illnesses for which cultures are taken,[1-4,9,10] and to be extremely rare (0–1%) in asymptomatic controls.[2-4] The incidence of *Campylobacter* seems to exceed that of *Shigella* and *Salmonella* in most studies of diarrheal illnesses; this suggests that it should *not* be considered an esoteric infection.[2-4,10,11]

The severity of illness caused by campylobacter infection varies widely[1] and those cases that are studied are probably skewed toward the more seriously ill since such patients seek medical attention more often and are more likely to have a culture taken. Little is known, however, of the pathophysiology of the infection. It most likely invades the bowel mucosa, but this has not yet been proven in man.[1] In one study, 12 of 16 patients with campylobacter infection had sigmoidoscopic examinations and ten of those showed evidence of colitis by granulation and friability of the mucosa.[3] However, sigmoidoscopic findings may not accurately reflect findings higher in the colon in regard to the extent or severity of disease. In a case of campylobacter infection where sigmoidoscopic findings were mild, barium enema revealed multiple ulcerations of the transverse colon.[3] No systematic studies of colonoscopic or barium examinations in patients with campylobacter infections have yet been done. This is probably due to the fact that the active phase of the disease is generally short-lived, and that most patients have recovered by the time most barium enemas would have been planned.

Antimicrobial treatment is available for campylobacter infection. The organism is usually sensitive in vitro to erythromycin, tetracycline, gentamicin, and chloramphenicol[1]; these drugs would not typically be chosen as empiric therapy for most bacterial enteric infections unless *Campylobacter* is specifically suspected. The choice of ampicillin in the case reported here typifies this problem. The organism is generally resistant to penicillins and cephalosporins, and often to sulfonamides and trimethoprim-sulfamethoxazole (TMP-SMZ) as well.[1]

It is often unclear whom to treat for campylobacter infection given the generally self-limited course of the disease, that is often resolved clinically within one week.[1] A recent double-blind trial of erythromycin for campylobacter infections showed no significant, clinical benefit in erythromycin-treated patients as compared to patients treated with placebo; the disease in general is acute and self-limited, and most patients improve on their own.[12] Stool cultures, however, may not become negative in these individuals for approximately five weeks without treatment,[11] whereas they promptly become negative in patients treated with erythromycin.[12] The clinical significance of this is uncertain.

The patient described here most likely would have improved without antibiotic therapy. Although there are no official guidelines, it is probably advisable to administer antibiotics to those patients with severe or prolonged symptoms, those at the extremes of age, or those with immune compromise.

Campylobacter infections are usually sporadic although they may occur in epidemics. Sources of infection may be contaminated food, milk, and water related to cattle, poultry, and pets. However, in many instances no identifiable source is found,[2] as seen in this case.

Interestingly, *Campylobacter* has also been shown to be involved in the exacerbation of symptoms in patients with known pre-existing ulcerative colitis and Crohn's disease with colonic involvement.[13] Thus, the relationship of campylobacter infection to colonic disease is even more complex and potentially confusing. The already inflamed colon may possibly provide an environment that is more permissive of infection by this organism. This may also explain the increased incidence of salmonella infection in ulcerative colitis.[14]

A heightened knowledge and clinical suspicion of *Campylobacter* should lead to its being found more often in patients with bacterial diarrheal disease, and the "waste basket" diagnosis of nonspecific colitis, or viral gastroenteritis, being made less often.

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Scaphoid megalourethra associated with nonobstructive dilatation of the posterior urethra

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Megalourethra is a rare congenital dilatation of the anterior urethra that results from faulty mesodermal development. Posterior urethral dilatation without posterior urethral valves is a separate entity that may be a part of prune belly syndrome. Isolated cases of idiopathic dilatation of the posterior urethra have also been reported. The association of anterior urethral dilatation (megalourethra) and dilatation of the posterior urethra has not been previously described in the same patient except in the presence of obstructing posterior urethral valves.[1] The following report is of a case in which megalourethra and dilatation of the posterior urethra coexist without bladder outlet obstruction.

CASE REPORT

A 12-year-old boy developed gross hematuria several hours after experiencing minor trauma to his right flank in gym class. He reported a long history of enuresis and engorgement of his penis during voiding. Physical examination was normal except for the presence of a grade II/VI systolic heart murmur. An intravenous urogram revealed bilateral hydronephrosis and hydroureter suggestive of reflux nephropathy. A cystogram (Fig 1) confirmed the presence of massive bilateral vesicoureteral reflux.

Voiding urethrography (Fig 2) revealed a markedly malformed urethra. The anterior urethra was dilated along its ventral aspect, resulting in a crescent-shaped deformity with the convexity directed ventrally. Marked saccular dilatation of the posterior urethra was also noted. There was no evidence of either obstruction or posterior urethral valves.

Urethral obstruction was also ruled out by subsequent urodynamic studies that showed strong detrusor hyper-reflexia with a coordinated external sphincter and normal flow. With 100 mL, the peak flow rate was 18 mL/s with no residual urine and no evidence of obstruction.

On cystoscopic examination there were no anterior or posterior urethral valves, no strictures or meatal stenosis, nor any other obstructive pathology noted. The patient underwent bilateral ureteral reimplantation. A second voiding cystourethrogram showed no vesicoureteral reflux. The anterior and posterior urethra remained markedly dilated.

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DISCUSSION

There have been 29 cases of classic megalourethra previously reported in the literature.[2] Hypospadias with associated megalourethra is a less severe variant of classic megalourethra that has been described in an additional 13 patients.[3,4] There are two varieties of megalourethra: fusiform and scaphoid. As its name implies, the fusiform type involves a spindle-shaped, diffuse dilatation of the penile urethra. This is caused by a lack of formation of the corpus cavernosa and corpus spongiosum, and it is associated with severe and often fatal anomalies. The more common scaphoid type of megalourethra is caused by the absence of the corpus spongiosum only. This results in the ventral dilation of the penile urethra as seen in the case reported here. The anomalies associated with scaphoid megalourethra are less severe than those of the fusiform variety.

FIGURE 1. A post-void film from a cystogram demonstrates bilateral vesicoureteral reflux.

FIGURE 2. A voiding film reveals a dilated crescent-shaped anterior urethra plus dilatation of the posterior urethra. There is no evidence of posterior urethral valves.

The radiologic diagnosis of megalourethra is based on the size and shape of the anterior urethra as seen on voiding urethrography. As was noted in the case reported, scaphoid megalourethra produces a characteristic crescent or sickle-shaped dilatation of the anterior urethra. Due to the ventral position of the absent corpus spongiosum, the convexity of the curve is always directed ventrally.

Fusiform megalourethra produces a spindle-shaped dilatation of the penile urethra on urethrography[5] and is thus readily distinguished from the scaphoid variety. Because of the complete loss of erectile tissue in fusiform megalourethra, even the distal anterior urethra becomes dilated; this is not typical of

scaphoid megalourethra.

The congenital anomalies associated with megalourethra include renal agenesis or dysplasia, hypospadias, urachal diverticulum, posterior urethral valves, upper tract dilatation, imperforate anus, and vesicoureteral reflux. These anomalies represent various forms of mesodermal dysplasia. Prune belly syndrome, the most severe form of mesodermal dysplasia, is present in 16% of all cases of megalourethra.[2] Once the diagnosis of megalourethra is reached, a careful uroradiologic investigation for these other associated abnormalities should be performed.

Dilatation of the posterior urethra without urethral valves or obstruction is also a manifestation of prune belly syndrome.[6] Four additional cases have been reported in boys without prune belly syndrome.[7] The dilatation has been thought to be a result of a congenital decrease in the amount of smooth muscle in the posterior urethra that results in a lack of muscular support.[7] Concomitant deficient development of prostatic tissue has been shown on histologic examination.[6] However, even in association with prune belly syndrome, there have been no prior reports of both megalourethra and nonobstructive dilatation of the posterior urethra occurring in the same patient.

As seen in the case presented here, the pan-urethral dilatation and visible swelling of the penis during voiding suggests an absent corpus spongiosum plus a deficiency of smooth muscle in the posterior urethra. These are both probably part of the same developmental anomaly of the mesodermal tissue.

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Pheochromocytoma and hypercalcemia due to ectopic production of parathyroid hormone

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Pheochromocytoma was first described by Frankel[1] in 1886, who observed bilateral neoplasms in a young woman who died suddenly. Although this tumor is rare, numerous cases of pheochromocytoma have since been reported in the medical literature, presenting a variable incidence of 0.1% to 0.01% in hypertensive patients and of 0.0001% in the adult population, as indicated by Van Heerden and associates.[2] Malignant pheochromocytoma[3] is unusual and represents from 1% to 15% of diagnosed cases. Dow and coworkers[4] reported extra-adrenal forms of pheochromocytoma in 30% of cases studied. Symptoms are due to the excessive release of epinephrine and norepinephrine, either separately or together, persistent or paroxysmal, or producing a constant or variable clinical picture.[5]

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During the last few years the concept of multiple endocrine neoplasia has been clarified, since the pathologic associations between endocrine pancreas, parathyroid, thyroid, adrenal, and pituitary glands were found to be part of specific syndromes. Therefore, with a case of pheochromocytoma all of the pathologic entities that are embryologically related to the pheochromocytoma—the organs containing APUD cells that originate from the neural crest and secrete polypeptide endocrine substances—must be examined.

The most common disorders affecting many endocrine glands are defined as multiple endocrine neoplasia types 1 and 2 syndromes (MEN 1 and MEN 2). MEN 1 syndrome (Wermer's syndrome) is associated with hyperparathyroidism in 90% of cases, pancreatic islet cell tumor (α_1- and β-cells and occasionally non-β-cells), and chromophobe pituitary adenoma in 60 to 70% of cases. The cortical tissue of the adrenal gland and the thyroid are involved less frequently.[6]

MEN 2 syndrome (Sipple's syndrome) defines a triad of hereditary neoplasms including pheochromocytoma, medullary thyroid carcinoma, and parathyroid hyperplasia. The latter syndrome, more precisely called MEN 2A, has a hereditary autosomal dominant character at high penetration. MEN 2A must be differentiated from MEN 2B syndrome, in which the incidence of hyperparathyroidism is rare, and which includes the association of ganglioneuromatosis and multiple mucosal neuromas.

Finally, associations of pheochromocytoma are uncommon with retinal angiomatosis (von Hippel's syndrome), cerebellar and medullary hemangioblastomas (Lindau's syndrome), chemodectomas (non-chromaffin paragangliomas), renal artery stenosis, hyperthyroidism, and hypertrophic gastritis (Menetrier's syndrome).[7]

FIGURE 1. Histology of left adrenal pheochromocytoma: cortical tissue with aspects of atrophy and neoplastic medullary tissue. (hematoxylin and eosin stain; original magnification X 100)

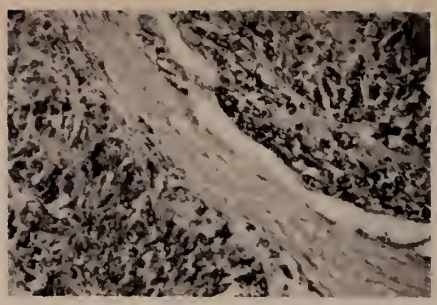

FIGURE 2. Histology of left adrenal pheochromocytoma: chromaffin medullary tissue. (Grimelius stain; original magnification X 400)

Case Report

A 67-year-old woman was admitted in April 1983 to the hospital for hypercalcemia due to suspected paraneoplasia that had been diagnosed during a previous admission to a Nephrologic Unit in October 1981 and treated at home with indomethacin. During this period the patient underwent oncologic studies that excluded osseous malignancies. Her family history was negative for blood disorders, hypertension, heart diseases, and endocrine disorders. In the past the patient had hypertension for about ten years that had been irregularly treated with diuretics, and she underwent a right radical mastectomy for breast cancer eight years before. The patient had been complaining of epigastric pain, dyspepsia, anorexia, and a weight loss of 22 lb for about two months prior to the actual admission.

On admission blood pressure was 170/110 mm Hg. Laboratory examination revealed a serum calcium of 12 mg%; serum phosphorus, 3 mg%; serum urea nitrogen, 104 mg%; serum glucose, 170 mg%; white blood cell count, 11,000/dL; sedimentation rate, 130 mm/h; serum alkaline phosphatase, 175 U (normal, 60 to 170 U); serum alpha$_2$-globulin, 19% and gamma-globulin, 21%; and parathyroid hormone (PTH), 0.11 ng/mL (normal, 0.1 to 1.3 ng/mL). Bone marrow aspirates and biopsy excluded hemopathies. Bone scans, radiographs, and endoscopy were negative. Computed tomography (CT) of the kidney showed left kidney ptosis. Ultrasonogram of the upper abdomen and abdominal CT scan revealed a mass of growth ascribed to the spleen, without diseased abdominal lymph nodes.

Two months later the patient underwent a laparotomy through a midline incision. A large retroperitoneal tumor was found—not associated with a normal-appearing spleen. After mobilization of a left colonic flexure, the left adrenal space appeared to be occupied by a round encapsulated mass that was apparently separated from the left kidney. A large left adrenal vein and the adrenal artery coming from the aorta were isolated, tied, and divided; the neoplasm was removed.

During the first hour of surgery the patient's blood pressure was between 180 to 200 mm Hg systolic and 120 to 130 mm Hg diastolic. After administration of labetalol 25 mg the blood pressure values decreased by about 20 mm Hg. Serious hypotension that occurred at the moment of adrenalectomy was immediately corrected by norepinephrine infusion.

The excised mass measured 12 X 7 X 7 cm, and the cut surface presented areas of necrotic tissue and cystic formations, with an evident capsular structure at the periphery. On microscopic examination, the neoplastic tissue was found to be crossed by fibrous and slightly vascular strands, and consisted of argyrophil cells. The pathologic diagnosis was left adrenal pheochromocytoma (Figs 1, 2).

The patient's postoperative course was uneventful except for mild dehydration due to a mineralocorticoid deficit that was corrected by adequate infusions. Her blood pressure remained stable at 130/90 mm Hg, serum calcium was normal on several postoperative measurements, and Vanillyl mandelic acid (VMA) excretion decreased from 12.7 mg/24 h in the early postoperative period to 5.6 mg/24 h on the day of discharge (normal, 1.7 to 7.4 mg/24 h).

In order to exclude a polyendocrinopathy type MEN 2, serum PTH was checked; it was normal. Furthermore, serum calcitonin —either basal or after stimulation with infusion of pentagastrin 0.5 μg/kg IV—was normal after three and five minutes. This test is considered indicative for the diagnosis of medullary carcinoma of the thyroid, as described by Wells and associates.[8,9] Serum gastrin, serum cortisol, and a radiograph of the skull for evaluation of the sella turcica were normal.

The patient was discharged on the 18th postoperative day, and is presently doing well.

Discussion

Considering the principles mentioned above, the hypercalcemia present in this patient prior to the operation but promptly resolved by removal of the neoplasm was difficult to explain.

After excluding the hypotheses of hyperparathyroidism due to parathyroid hyperplasia or osseous changes due to bone metastases, we evaluated the possibility that secretion of PTH or a substance similar to PTH was intrinsic to the neoplasm. Swinton and colleagues[10] in 1978 reported on a case of hypercalcemia corrected by the removal of a pheochromocytoma. Similar observations were reported in the medical literature by Kukreja and coworkers[11] in 1973, Ghose and associates[12] in 1976, and Gray and Gillan[13] in 1976. Kukreja and coworkers hypothesized that hypercalcemia was due to hypersecretion of PTH consequent to catecholamine excess. This hypothesis was contested by Miller and colleagues.[14]

Demonstration of PTH-like activity in the neoplastic tissue at similar levels to those described by Buckle[15] in 1974 in the ectopic PTH syndrome (0.75 to 8.9 μg/g of dried tissue) suggested that hypercalcemia was due to a PTH or PTH-like peptide substance produced by a pheochromocytoma.

Homogenized tumor tissue was studied for PTH activity, producing a value of 75.4 ng/mL (equivalent to PTH 1-84). The COOH− terminal fragment (PTH 65-84) was checked by using the radioimmunoassay method with specific antiserum (Immunoclearcorpuration). While the value obtained from the homogenized tissue cannot be related to the value reported by Buckle because of different laboratory methods, its pathologic significance is clear because it was obtained from tissue lacking PTH-like activity.

The conclusion drawn here is similar to that of Fairhurst and Shettar[16] in that some cases of hypercalcemia, when certain known pathologic entities are carefully excluded, may result from an ectopic production of PTH-like polypeptides.

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Aspergilloma producing painful ophthalmoplegia

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Aspergillus infections may manifest in many ways and are a particular threat in immunocompromised patients. Painful ophthalmoplegia is usually caused by either neoplastic or vascular involvement of the retroorbital area, trauma, or infection. The syndrome of painful ophthalmoplegia consists of orbital and periorbital pain with variable involvement of cranial nerves two, three, four, six, the first division of the fifth, and periarterial sympathetic nerves. This is most often due to vascular disease such as aneurysm of the carotid artery,[1] tumor,[2] trauma, or infection[3] involving the cavernous sinus or superior orbital fissure.

In the case presented here, painful ophthalmoplegia was caused by aspergillus infection in a patient who had lymphatic leukemia with many causes of depressed immune function.

CASE REPORT

An 83-year-old pale, alert, ill-appearing man was admitted to the hospital with eye pain and severe nosebleeds. He had been blind for many years due to glaucoma and had stable chronic lymphocytic leukemia for two years. Four months earlier he complained of increasing weakness and right orbital pain. The hematocrit was falling and the white blood cell count was rising; treatment with chlorambucil was started.

Three months prior to admission, when the patient was hospitalized for pneumonia, computed tomography (CT) to evaluate his eye pain demonstrated normal sinuses and boney structures of the head and thickening of the optic nerves. One month before admission neurologic examination revealed limitation of upward gaze and of abduction past the midline in the right eye. Downward and medial gaze in this eye were normal as were all movements of the left eye. Corneal reflexes were normal bilaterally and there was no ptosis. Pain sensation over the right forehead was reduced. The patient had undergone surgery for cataracts and glaucoma; there were no pupillary reactions. Funduscopic evaluation was impossible because of old corneal opacities. Ear, nose, and throat examinations were normal. Prednisone therapy was initiated and the eye pain was promptly and nearly completely relieved. The eye movements remained unchanged and the prednisone dose was reduced.

Two weeks before the present admission the patient was hospitalized for an episode of severe nasal bleeding that was easily controlled with nasal packing. His eye pain increased, however, and the prednisone dose was raised. One week following discharge from the hospital, major epistaxis recurred and the patient was readmitted.

On admission the patient's temperature was 98.7°F; pulse, 94/min; and blood pressure, 130/70 mm Hg. There was ptosis of the right eye which was fixed in a downward gaze, and there was active nasal bleeding. Corneal reflexes were present bilaterally and left eye movements were normal. Bilateral intraocular pressure was also normal. There was no proptosis, and there were no visible masses in the oral or nasal pharynx. No lymphadenopathy or hepatosplenomegaly was noticed.

Laboratory examination revealed the following: hemoglobin, 10.9 g/dL; white blood count, 107,000/μL with 97% lymphocytes, 2% segmented, and 1% band neutrophils; and platelet count, 357,000/μL. Prothrombin time, activated partial thromboplastin time, electrolytes, and urine analysis were normal.

CT scan of the head revealed a soft tissue density in the sphenoid sinus that extended into the right cavernous sinus. Radiotherapy to the paranasal sinuses, orbit, and nasal cavity was begun. Recurrent epistaxis was controlled with posterior nasal packing. Therapy with cephalothin was instituted. The patient's temperature increased to 103°F and a chest radiograph revealed a new right lower lobe infiltrate. Blood cultures grew *Enterobacter aerogenes*, and ticarcillin and tobramycin were begun.

The patient became obtunded and left hemiparesis developed. CT scan demonstrated an infarct in the right temporal lobe in addition to the previously noted mass in the sphenoid sinus. A lumbar puncture revealed clear fluid with an opening pressure of 190 mm; glucose was 58 mg/dL and the total protein was 65 mg/dL. There were 4 red blood cells and 272 white blood cells/μL of which 99% were polymorphonuclear leukocytes and 1% lymphocytes. Chloramphenicol and dexamethasone were added. Radiation therapy was stopped after the administration of a total dose of 1,200 rad.

The patient remained febrile throughout the rest of his hospital course. Cerebrospinal fluid and multiple blood cultures were negative. Urine culture revealed 10,000 colonies/μL of *Candida albicans*. On the 19th hospital day the patient became comatose and on the 22nd hospital day he died. Post mortem examination revealed a dense mass of *Aspergillus hyphae* forming the density in the sphenoid sinus, invading through bone into the orbit, and encasing the optic and oculomotor nerves. Numerous aspergillae were found in the lungs. Lymph nodes revealed the uniform findings of chronic lymphocytic leukemia.

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Discussion

Initially, in the absence of findings on both ear, nose, and throat examination and CT scan, the syndrome of idiopathic granulomatous inflammation of the cavernous sinus as described by Tolosa[4] and Hunt[5] was entertained. The Tolosa-Hunt syndrome[3,6,7] is characterized by attacks of steady, boring eye pain and ophthalmoplegia, lasting days or weeks, occurring at intervals of months or years, variably involving the second through sixth cranial nerves, and spontaneously remitting, sometimes with residual deficits. There is no systemic reaction, studies yield no evidence of involvement outside the cavernous sinus, and there is dramatic response to steroid therapy.

Although initially considered because of the absence of findings on CT scan, the diagnosis of Tolosa-Hunt syndrome soon became untenable in this immunocompromised patient suffering from chronic lymphocytic leukemia. The presence of a sphenoid sinus mass suggested the urgent need for tissue diagnosis. Both otolaryngeal and ophthalmic surgeons were extremely reluctant to undertake surgical exploration of this heavily bleeding and bone eroding lesion.

Accordingly, it was decided to treat a possibly radiosensitive lesion with radiation therapy in the hope of inducing a remission. Risk factors for the development of infection and sepsis, especially fungal, were already numerous. The patient had lymphatic leukemia and had received alkylating chemotherapy. He was receiving corticosteroids and radiotherapy, and there was tissue necrosis with drainage impeded by a posterior nasal packing. Numerous factors thus conspired to provide an ideal setting for the development of severe invasive and disseminated fungal disease. Treatment, promising only a minimal chance of success, would have required antifungal therapy in addition to wide surgical debridement that would have been impossible, given the location of the disease.

Fungal infections, and among these, aspergillus, are common in malignant disease.[8,9] Aspergillus may invade the paranasal tissues[10] as well as numerous other sites,[11] and it may be fulminant in states of immune suppression[12] or leukopenia.[13] Aspergillus involvement of retrobulbar structures may be a cause of the syndrome of painful ophthalmoplegia.

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CORRECTION

In a recent issue of the *Journal*, the article entitled, "Disseminated histoplasmosis in a man with AIDS" (1985; 85:664–665) contained an error. The first sentence of the last paragraph should read as follows: In a patient with a positive serologic or virologic test for HTLV-III/LAV, disseminated histoplasmosis—not confined to the lungs or lymph nodes—diagnosis by culture, *histology*, or antigen detection has now been included in the revised definition of AIDS by the Center for Disease Control.[4]

Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

Prolonged mild diarrhea caused by Campylobacter

TO THE EDITOR: *Campylobacter* is a cause of bacterial gastroenteritis in children and adults. Campylobacter enteritis is usually a self-limited illness with symptoms that resolve in less than two weeks, even without antibiotic therapy.[1] The following is a report of a child with mild diarrhea of three months duration caused by *Campylobacter.*

Case Report. An 11-month-old girl was referred to the pediatric gastroenterology clinic because of persistent diarrhea for three months duration. The patient had between two and six loose, watery stools per day that were frequently mucoid but never bloody. The patient had no spiking temperatures, vomiting, or abdominal pain. She had a good appetite and continued to grow well during that time.

The patient weighed 24 lb 4 oz (90th percentile) and her height was 30½ in (75th to 90th percentile). She was in no distress. Her abdomen was soft, nontender, and without organomegaly or masses. Rectal examination revealed stool that was negative for occult blood. The rest of the physical examination was unremarkable. The patient was then started on a high fat diet for chronic, nonspecific diarrhea.

Stool for ova and parasites was negative; stool culture was positive for *Campylobacter jejuni.* The patient was treated with erythromycin ethylsuccinate, 40 mg/kg/d for seven days. After five days of treatment, the diarrhea ceased and the patient was having normally formed stools. There have been no recurrences of the diarrhea for the following year.

Discussion. The most common symptoms associated with enteritis caused by *Campylobacter* in children are fever, diarrhea, and bloody stools that occur in approximately 90% of patients. Abdominal pain is present in about 60% of patients and vomiting occurs in about 30%.[2]

Usually campylobacter enteritis causes an acute, self-limited illness. Few cases of long-lasting diarrhea due to *Campylobacter* have been reported.[3,4] Chronic diarrhea in children is usually attributed to other causes.

Most young children with chronic diarrhea and yet gain weight have chronic, nonspecific diarrhea of infancy. The onset of symptoms usually occurs between six and 30 months of age with the development of between three to six loose stools with mucous per day. Resolution usually occurs by approximately 39 months of age. A high fat diet has been shown to decrease the frequency of diarrhea in this condition.[5]

The symptoms of the patient described here were compatible with chronic, nonspecific diarrhea. She was having from two to six loose, mucousy, nonbloody stools per day. There was no complaint of abdominal discomfort. The patient continued to grow well during this time period. After her stool culture was positive for *Campylobacter,* she was treated with erythromycin. The diarrhea stopped during treatment and there has been no recurrence.

Campylobacter is a cause of prolonged, mild diarrhea in childhood and may cause the same symptoms as chronic, nonspecific diarrhea. All children with chronic diarrhea should have a rectal swab[6] or preferably a stool culture to rule out the possibility of campylobacter enteritis.

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See also pp 23–23.

School bus safety

TO THE EDITOR: In October 1985 an 11-year-old boy was killed while riding on a school bus in Putnam County, New York. Since it is almost certain that a seatbelt would have saved the child's life, there have been renewed efforts to equip school buses with seatbelts. These efforts are supported by evidence that seatbelts on school buses would save lives and reduce injuries.[1] New York State now leads the nation in the number (17) of individual school districts that have initiated seatbelts on school buses. However, in another area of school bus safety New York lags far behind most other states.

New York is one of only a few states that has not conformed to the 1977 National Highway Traffic Safety Administration's recommendation that no child be allowed to stand on a school bus. "Standees" are extremely vulnerable in the event of an accident. New York State not only permits this dangerous practice, but actually encourages standees through its reimbursement policy for transportation costs. Buses must be completely filled—including 20% standees—to receive full state aid. The effect of this most unenlightened policy is that those school districts that attempt to provide reasonable safety for their children by eliminating standees and requiring seatbelts are financially penalized.

In a review of pupil transportation Charles and Shelness noted, "The ITTE/UCLA bus crash research proj-

ect has now added indisputable evidence to what must surely have been only too obvious all along: in the event of a sudden stop, standees are in danger of being flung the full length of the aisle or of being hurled against one another or on top of seated pupils. Standees are therefore not only more likely to be injured themselves, but also endanger seated passengers. Any seat affords some protection, while standees have none."[2] New York State has unfortunately ignored this important data. Had the bus in which the child was killed been filled to capacity, including standees, it is likely that an even greater tragedy would have occurred.

New York State has taken the lead in other areas of school bus safety, such as requiring high-back seats. Although more school districts in New York have seatbelts on school buses than in any other state, this is solely the result of local efforts rather than statewide support. Indeed, the present state reimbursement policy that rewards standees is counterproductive to a requirement for seatbelt use on school buses since the latter mandates that standees be eliminated. I urge New York to change this policy and follow other states in eliminating the dangerous practice of standees. In order to bring the school bus safety program up to acceptable standards the state must also require that all new buses be purchased with seatbelts. Safety standards should be uniform throughout the state; every child deserves the benefit of the safest bus travel available.

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Note: Leon Blum, the editor's 5-year-old assistant, also wonders why children are told to buckle up in cars but not on school buses. He adds, "Why does the driver have a seat belt and the kids do not?"

Silicone breast injections

TO THE EDITOR: Silicone injections into the breast do indeed cause a variety of unpleasant complications. One can have no quarrel with the observations and conclusions drawn by Cruz and colleagues (1985; 85:599–601) save one. The lead sentence of their article states that intramammary silicone injections have become popularized. This is not true. Silicone injection has been performed, and has also led to complications as described. However, it has never been either a popular or approved method of breast augmentation.

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Malpractice in New York State

TO THE EDITOR: I wanted to let you know how the malpractice situation in New York State is viewed by a newly-trained, Board-certified family physician. I came to New York State after my medical training because my family is located here; they have lived in Syracuse for 100 years. My dream was to open an office in an underserved rural location in New York. I found and renovated an office in Fulton, beginning in September 1984. Much to my surprise, the increase in malpractice insurance premiums was announced the following December and by that time it was bit too late to turn back.

The malpractice rates for a family doctor in Pennsylvania where I trained are $2,200 per year. The malpractice rates for a family doctor in Vermont are $400 per year. I could not believe that family physicians in Syracuse who were not even performing obstetrics were paying $8,000. I also could not believe that something was not being done about this.

A family physician in a rural area earns about $40,000. Even though the orthopedic surgeons, obstetricians, gynecologists, and neurosurgeons have been the most vocal about the increase in premiums, the malpractice crisis has probably hurt family physicians and pediatricians the most. These two are the lowest paid types of medical specialist. One third of the population of the United States is located in rural areas, and they have only 12% of the nation's doctors.

In New York State there has been a 27% decrease in the number of family physicians over the past ten years. New York State graduates approximately 100 family physicians each year. These physicians are well aware of the problem of practicing in New York State. I serve as a family practice student advisor for Upstate Medical Center and feel that the Governor would have much to learn by listening to how medical students training in New York State feel about the problems physicians are facing with the malpractice crisis.

On June 28, 1985 I closed my office in Fulton because I could not financially survive the increase in malpractice premiums. My patients in this area could not afford to pay an increased fee for office visits and approximately 20% were on Medicaid (some 20% of Americans have no form of health insurance). I saw some people who could not even afford my usual fee of $20 for an office visit. I did not use a collection agency. I always told my patients to pay what they could, and the rest would be forgotten. I did not have the heart to turn them away from care and would rather close my office than treat only the wealthy and insured.

Recently, the New York State legislature has approved an increase in funding for family practice residency programs from $1.5 to $2.5 million. I find this somewhat ironic. Although they are educationally supporting the residents on one hand, they are also creating an atmosphere in which it is impossible to practice medicine after graduation in New York State on the other. I think it is very kind of our legislature to train family physicians for other states, although I am not sure that this would make the taxpayers happy.

Because I sit on the Membership Committee of the New York State Academy of Family Physicians, I would like to share with you my concern regarding members leaving New York State (Table). This survey is for the

TABLE. New York State Academy of Family Physicians Physician Loss Survey January 1985–May 1985

27 Active members have moved out of New York State
18 Responses
- 11 Left for personal reasons, including malpractice
- 1 Left for a better opportunity
- 5 Left because of malpractice rates
- 1 Left for a military commitment

17 Resident members have moved out of New York State
9 Responses
- 4 Left because of National Health Service Con. Commitment
- 5 Left because of malpractice rates

first six months of 1985 and includes only Academy members. Letters were sent to all residents and active members who have moved out of New York State. As you can see, 16 active members and five residents left New York State stating malpractice costs as a reason. Our Academy's Executive Secretary, Donna Lewis, feels that we are easily going to lose 50 physicians (family doctors) from New York State this year. This is quite serious owing to the fact that we are only graduating 100 family physicians per year. Who is to replace the family physicians who are infirm, retired, or dead? We lose more ground every day.

Our State Assembly, out of self interest, has valiantly defended the rights of a few patients to sue for enormous amounts. However, this has jeopardized the rights of many thousands of rural upstate New Yorkers to obtain accessible and affordable health care. For them, the physician shortage will worsen. Where is the public interest being served?

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Extensive calcification of the thyroid gland

TO THE EDITOR: Calcification of thyroid tissue is not an uncommon finding in papillary carcinoma of the thyroid. The psammoma bodies appear as lamellated configurations on radiographic examination. Extensive calcification of the thyroid gland, however, is rare and when present usually indicates a benign disease.

Case Report. An 81-year-old white woman was admitted to the hospital for management of malignant melanoma involving her left lower limb. The patient was unable to give any history concerning her thyroid status because of senile dementia. Her nursing home records did not reveal any prior thyroid history.

On physical examination only the superior portion of the thyroid was palpable on swallowing; the remainder of the gland was substernal. The palpable portion of the thyroid was hard, lobulated, and nontender. Widespread calcification of the thyroid was noted on chest radiograph (Fig 1).

FIGURE 1. Chest radiograph showing calcification of the thyroid.

Thyroid function studies were as follows: thyroxine (T4), 6.9 μg/dL (normal, 5.5 to 16.0 μg/dL); T_3 resin uptake, 27.3% (normal, 24 to 36%); and thyroid stimulating hormone (TSH), 2.9 μU/mL (normal, 1.0 to 8.0 μU/mL). Antithyroglobulin antibodies were negative and antimicrosomal antibodies were positive, 1:200 (normal, <1:10); 24-hour radioactive iodine uptake (^{131}I) of the thyroid was 17% (normal, 10 to 35%). The thyroid image (Fig 2) showed a large cold area in the right lobe. The serum calcium was 9.1 mg/dL (normal, 8.5 to 10.5 mg/dL); serum phosphorus, 3.5 mg/dL (normal, 2.5 to 4.5 mg/dL), blood urea nitrogen, 14 mg/dL (normal, 8 to 23 mg/dL); and creatinine, 0.7 mg/dL (normal, 0.6 to 1.2 mg/dL). The electrolytes, total protein, and alkaline phosphatase values were normal.

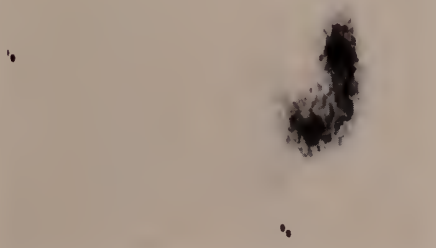

FIGURE 2. Thyroid image showing a cold area in the right lobe.

Discussion. The deposition of calcium salts in damaged tissue, despite normal serum levels of calcium and normal calcium metabolism, is known as dystropic calcification.[1] This phenomenon is encountered in coagulation and liquefaction and enzymatic necrosis whenever necrotic tissue persists for a long period of time. This patient perhaps had an episode of hemorrhage into an adenoma within the right lobe of the thyroid with calcification of the resulting necrotic tissue.

Segal and associates[2] describe criteria for malignant lesions of the thyroid on soft tissue roentgenography. These calcifications are poorly marginated, hazy, not dense, and about equal in size. They are usually grouped either in streaks or in a nebular formation within a limited area that does not have a calcific, well-defined rim. In contrast, opacities appearing in benign thyroid lesions are usually densely calcified, sharply defined, well marginated, and of varying sizes. When grouped together, opacities in benign thyroid lesions are surrounded by a calcific rim. However, they are usually spaced haphazardly. The appearance of the calcification on chest radiograph of the patient discussed here is suggestive of a benign thyroid lesion. However, thyroid malignancy cannot be completely excluded[3] in this situation. Fine needle biopsy of the right lobe of the thyroid of this patient might have resolved this diagnostic problem. However, because of the substernal location of the thyroid, the uncooperative behavior of the patient, and the more urgent problem of managing the malignant melanoma, needle biopsy was not attempted.

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In the September issue the *Journal* began publishing the list of physicians who have generously contributed to the campaign to inform the public about the crisis in medical liability litigation. The names of additional contributors are listed below.

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THE HEART: PHYSIOLOGY, METABOLISM, PHARMACOLOGY, THERAPY

By Lionel H. Opie, MD. 392 pp, illustrated. London, Grune & Stratton, Ltd., 1984. $55.00 (hardcover)

This survey text in cardiology is intended to explain the principles of cardiac function, both normal and pathologic, to a wide audience "including fellows in cardiology, interns and residents, medical registrars, as well as students of physiology, pharmacology, or medicine." The primary author, Dr Lionel H. Opie, is a well-established investigator who has an international reputation in cardiac research, and is the Editor of the *Journal of Cellular and Molecular Cardiology*. As such, he has unique credentials for writing a book such as this. In addition, several of the chapters were prepared with the help of consultants with special expertise in their fields. These consultants were Drs Wieland, Gevers, Winifred Naylor, and Radovan Zak. Thus the authoritativeness and qualifications of the authors are well recognized, and the book should represent a useful contribution to the medical literature.

The book is divided into four sections. The first section reviews cardiac histology and basic myocardial physiology at the cellular and subcellular level. The second section deals with cardiac energy metabolism, coronary flow and oxygen demand, and mechanical function of the ventricles. The third section is concerned with the pharmacology of the commonly used cardiovascular drugs, including autonomic agonists and antagonists, vasodilators, "calcium antagonists," digitalis, and other positive ionotropic agents. The final section is entitled, "Heart disease: Pathophysiology and Pharmacological Therapy," and covers topics including hypertension, angina pectoris, myocardial infarction, arrhythmias and antiarrhythmic agents, congestive heart failure, cardiomyopathies, and valvular heart disease. Thus, the scope of this book is comprehensive. It is written to present the authors' views on each topic covered in a simple and easily understandable way. The text is supplemented and reinforced by many drawings and illustrations. Overall, the material is presented in a didactic manner, such that the book resembles a very detailed set of lecture notes from a course in cardiovascular medicine. As such, this book should accomplish the authors' stated objectives.

The only significant drawback of this book is that by being didactic, it oversimplifies some controversial points. Additionally, the references provided are selected, rather than comprehensive. Thus, if the reader wants to investigate a topic in depth, he will have to look elsewhere to find detailed explanations and citations to many of the original papers in the scientific literature.

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BEDSIDE CARDIOLOGY

Third Edition. By Jules Constant, MD. 458 pp, illustrated. Boston, Little, Brown and Co., 1985. $39.95 (clothcover)

In this era of high technology in medicine, it is refreshing to review a book that concerns itself directly with the patient. *Bedside Cardiology* discusses the details of taking a thorough cardiac history and performing a skillful cardiovascular physical examination. The author uses a question-and-answer format, with the answers graded according to the experience of the reader—medical student, resident, internist, and cardiologist. Thus it is an excellent teaching tool for all those who are interested in learning all that can be obtained directly from the patient with a cardiac problem.

At one time medical students had been taught that 50% of diagnoses could be made from a well-taken history, and another 25% from a carefully performed physical examination. Many doubt that the percentages have changed very much, even with all of the technical advances available today. Thus, a text devoted to facts obtainable from the patient continues to be most pertinent.

This third edition of Constant's textbook reflects the many advances in the understanding of cardiac physiology, pathophysiology, and diagnosis that have occurred in the nine years since the second edition was published. Considerable technical information from phonocardiograms, apex cardiograms, and echocardiograms have been used to support the interpretation of physical signs. In addition to a chapter on history-taking, there are chapters on the following subjects: cardiac clues from physical appearances; peripheral pulses and pressures; jugular pressure and pulsations; inspection and palpatation of the chest; diagramming and grading heart sounds and murmurs; the stethoscope; each one of the four heart sounds; the opening snap; systolic ejection and regurgitation; diabetic murmurs; prosthetic valve sounds; and systolic time intervals. A means of estimating an ejection fraction on physical examination is described. Each chapter is supported by an impressive bibliography.

The question-and-answer format deserves emphasis. It allows students to test their ability to answer questions before looking at the authoritative information, and it suggests questions to the instructor that may be used in teaching students and house staff. Certainly, asking questions helps students to identify the kinds of topics that the instructor may consider significant. Verbalizing the answers helps to reinforce the student's memory of the information provided by the instructor's query. Examples of questions provide a dynamic explanation of its usefulness: "What are the common causes of a false rise in the height of jugular pulsations with abdominal compression? What left parasternal movement should make you doubt the presence of an Ebstein's anomaly? How does a stiff mitral valve, as in mitral stenosis, affect the duration and pitch of the M_1? When will a tricuspid os be present in the absence of tricuspid stenosis?"

Most examinations in internal medicine and cardiology contain questions similar to those presented in the text, adding another parameter of usefulness to the book. All in all, this book is a valuable addition to a cardiology library.

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CLINICAL ECHOCARDIOGRAPHY. CASE STUDIES: HEMODYNAMIC AND PATHOLOGICAL CORRELATIONS

By Jose Missri, MD. 420 pp, illustrated. New York, Yorke Medical Books, 1984. $45.00 (hardcover)

The theme and purpose of this book—one of many in the burgeoning field of cardiac ultrasound—is to demonstrate the clinical application of echocardiography as a tool for improving patient care. The author is the director of both a coronary care unit and a noninvasive laboratory and undoubtedly has had exposure to both the research considerations and the clinical use of echocardiography. This is a field in which many experts have produced several very useful and comprehensive clinical texts. Thus adding another book is a considerable challenge.

The book's organization is similar to many others in the field. It begins with the physical principles of echocardiography and the well-described relations of echocardiographic anatomy. M-mode, 2-D, and pulsed doppler are described both in clinical application and relevant physics. The book's contents, on a chapter-by-chapter basis, cover the range of applications of this modality. Representative chapters include aortic and mitral valve disease, tricuspid valve disease and cardiomyopathy, ischemic heart disease, pericardial disease, and endocarditis as well as prosthetic valves, congenital heart disease, aortic disease, and cardiac tumors.

Each of these chapters is introduced by a clinical problem involving a patient and the relevant anatomic area. The author then proceeds to show the application of echocardiography in the diagnosis and treatment of the patient. The author's style is lucid, pleasant, and easy to read. However the contents are not in any way remarkable and do not represent any new data in this field. Rather, the physiologic and anatomic correlations are presented on a level somewhat more superficial then many standard text books. This is due in part to the relatively brief size of the text and to the inclusion of case reports which limit in-depth discussion.

Technically the book is well produced with a typeface that is easy to read but with illustrations that are not in any way remarkable. The illustrations do not significantly add to the text and in many cases, because they are the "stop frame" type of 2-D photo, much information is lost.

If this book were to be compared to other publications in the field it would be fair to say that it adds nothing new and that it lacks the depth that standard textbooks such as those of Feigenbaum and Gramiak afford. In addition the references are limited in number and somewhat superficial. They tend to include secondary sources (such as other textbooks) rather than primary sources.

This text might be helpful and interesting to medical students and perhaps to junior house officers. Senior house officers, cardiology fellows, and practicing cardiologists would certainly be better served by a text with greater breadth and depth and with a richer fund of references. That being the case, I believe that this text falls short of the author's goal of increasing our understanding of the clinical utility of this already widely used diagnostic mode.

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THE PARENT'S PEDIATRIC COMPANION

By Gilbert Simon, MD, Marcia Cohen. 378 pp. New York, William Morrow and Co., 1985. $17.95 (hardcover)

On the front cover of this book is a quotation by Dr Benjamin Spock: "If you have any tendency to worry about physical conditions in your baby or child—and who doesn't?—this is the encyclopedia to have on your shelf." I agree, with only slight reservation. The book is well organized, well documented, and well written. Its purpose is to serve as a guide for parents to explain the many physical and behavioral conditions that are part of the natural growth and development of a child from birth through adolescence. The book accomplishes this purpose and the authors are to be congratulated for a job well done.

Gilbert Simon, MD, an experienced practicing pediatrician, and Ms Marcia Cohen, with the assistance of a number of distinguished physicians who reviewed the various sections of the book dealing directly with their own specialties, have produced an extremely useful addition to the literature.

The book is divided into three sections: the newborn (from birth to six months), the pre-schooler (from six months to six years), and the older child (from six to sixteen years). In each section the authors describe the physical changes that normal growth produces, the dynamic normal functions of the body, and various problems that may arise at each stage. Clear, reliable, and well-researched explanations are given for many of the physical and behavioral conditions that parents face in raising their children.

As a practicing pediatrician myself, I understand the many anxieties of parents, especially the first-time parents—from birth marks to the number of bowel movements, to turned-in feet, to disappearing penises, to oozing navels, and on. Mothers and fathers are entitled to accurate and careful explanations for any and all of the normal conditions that affect their children. However, in the rush of a pediatrician's office, very often it does not work that way. This is the main value of the book. At the end of each subject discussed, references are cited from the medical literature. This is quite useful for the pediatrician but in my opinion not appropriate for most parents. Since the proposed readership of this book is parents, I cannot understand why the authors chose to include such an extensive reference list from pediatric journals and texts. Very few parents have either access to medical libraries or the expertise to read and understand the articles. Further, the subjects covered in the book, primarily normal physical conditions, do not require medical reference documentation, at least from the parent's point of view.

Almost without exception I found myself agreeing with everything that was written; but I question two statements. In their discussion about "growing pains," the authors state that in such cases, the doctor will probably find that the child's feet are "flatter than pancakes." This has not been my experience. As for the transient personality changes following a significant head injury (post-traumatic syndrome), the statement is made that up to 30% of children developed this after a head injury. In my experience and according to my review of the subject, these personality changes occurred much less often than 30% of the time.

This book achieves the authors' stated objectives and has become a most welcome addition to my medical library. I believe it would be useful for pediatric residents and for practicing pediatricians. For those knowledgeable parents who require detailed explanations about what is going on with their children beyond the all too often "it is

normal, so don't worry about it" from their pediatrician, this book would also serve a useful purpose.

I found only one typographical error but it is a beaut! The index under "Convulsions" lists "breast holding" instead of "breath-holding."

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TE LINDE'S OPERATIVE GYNECOLOGY

Sixth Edition. By Richard E. Mattingly, MD, John D. Thompson, MD. 938 pp, illustrated. Philadelphia, J.B. Lippincott Co., 1985. $95.00 (hardcover)

The field of operative gynecology is an extremely large one for either one or two authors to handle. Although the two editors of this text have wide experience in the field, they have selected outstanding specialists to write about specific topics. The book is built on the basic work of Richard W. Te Linde who was the sole author of the first three editions. The history of the development of pelvic surgery is slanted towards the Johns Hopkins "School of Gynecology." All of the pictures illustrating this section are from that group, including that of Papanicolaou; his basic innovations in cytology have saved more lives than the efforts of many gynecologic surgeons. Ascheim and Zondek should also have been included for their discovery of the pregnancy test, Gemzell and Lunenfeld for the use of human menopausal gonadotrophin, and Yalow and Berson for the development of radioimmune assay.

The anatomy of the female pelvis is clearly described. Included are several excellent illustrations of the vascular bed. However, there are no pictures showing the course of the ureters.

In the chapter on postoperative care there is an excellent summary of venous thrombosis. The determination of who is in a high risk category for this complication and how to treat it prophylactically with low doses of heparin or therapeutic heparin and warfarin sodium are fully explained. The clinical profile, the extent of surgery, and the diagnosis of the lesion all help to determine the analysis of risk. The techniques of hysterectomy for benign disease and myomectomy are described in great detail, as are the historic treatises of Bonney and Rubin on myomectomy and Richardson on hysterectomy. Surgery for anomalies of the müllerian ducts is well detailed. Vertical and lateral fusion of the müllerian ducts are presented in detail with excellent accompanying illustrations. The many surgical techniques for reconstruction of an absent vagina are also listed and detailed. The Jones metroplasty for correction of the uteral septum and the classic Strassman metroplasty are described with accompanying drawings. The new technique via hysteroscopy for cutting a uterine septum is not included. Reconstruction of the fallopian tube, laparoscopy, tubal sterilization, and ectopic pregnancy are covered in a systematic fashion. The higher incidence and advantages for early diagnosis of ectopic pregnancy by such means as laparoscopy, sonography, and quantitative β-HCG values are well presented. The newer test for HCG—highly sensitive and more specific than the Beta Sub Unit—include the two monoclonal antibodies for quantitative and qualitative determinations; this large category of recent tests is omitted.

The chapters relating to the intestinal tract in gynecology, the appendix, curettage of the uterus, abortion, surgery for relaxation of the vagina, stress incontinence, and vesicovaginal and rectovaginal fistulas are extensively described and appropriate references are cited. Neurologic and urologic studies are detailed. The surgical drawings for the Marshall-Marchetti-Krantz and Goebell-Stoeckel sling operations cover the finest detail of the procedures. Those residents who have never seen these procedures performed should read the description of the operative procedure the night before surgery. The fourth and final segment of this opus on operative gynecology includes malignant diseases.

The authors touch upon the psychologic aspects of pelvic surgery. These are of great importance, particularly with women who believe that such surgery threatens their sexual identity. Carcinoma of the cervix and uterine fundus, and neoplastic tumors with associated chemotherapy and radiation are included. The chapters include the standard classifications and descriptions of the preferred operative procedures, and also include the follow-up in such procedures performed throughout the world.

This book had successfully covered the entire field of gynecology with excellent references for each chapter; it also includes the related area of informed consent. In a standard consent form, the paragraph reads: "I understand that the practice of medicine is not an exact science and that diagnosis and treatment involve risks of injury or even death." If the patient is frightened with such a statement, there is the chance that operative risks will increase, as will operative complications. Informed consent—basically considered a legal term—is difficult to achieve unless patients, like physicians, attend four years of medical school. Drs Di Saia, Creasman, Townsend, and Nelson have contributed information concerning malignant disease; these sections should be included as special reading for students of oncology. Ball's *Gynecological Surgery and Urology* is a classic in the same area as this book, but the last edition is outdated. The present book by Mattingly and Thompson should be the standard text for residents and gynecologic fellows in the United States.

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CARDIOLOGY

Cardiology 1985. Edited By William C. Roberts, MD. 500 pp, illustrated. New York, NY, Yorke Medical Books, 1985. $55.00 (hardcover)

DERMATOLOGY

Illustrated Encyclopedia of Dermatology. Second Edition. By Lionel Fry, MD, Fenella T. Wojnarowska, MD, Parvin Shahrad, MD. 576 pp, illustrated. Oradell, NJ, Medical Economics Co, 1985. $29.95 (casebound)

EMERGENCY MEDICINE

Emergency Problems in the Elderly. Edited by Edward P. Hoffer, MD. 256 pp, illustrated. Oradell, NJ, Medical Economics Co, 1985. $22.95 (hardcover)

Comprehensive Management of Respiratory Emergencies. Edited by Barry E. Brenner, MD. 398 pp, illustrated. Rockville, MD, Aspen Publications, 1985. $61.50 (hardcover)

FAMILY PRACTICE

Principles of Family Systems in Family Medicine. Edited by Sergio Henao, MD, Nellie P. Grose, MD. 438 pp. New York, NY. Brunner/Mazel Publishers, 1985. $40.00 (hardcover)

HEALTH CARE

Malpractice: Managing Your Defense. By Raymond M. Fish, MD, Melvin E. Ehrhardt, MD, Betty Fish, MSW. 226 pp. Oradell, NJ, Medical Economics Co, 1985. $24.50 (hardcover)

DRG. Survival Manual for the Clinical Lab. Edited by Robert J. Fitzgibbon, Bernard E. Statland, MD. 264 pp, illustrated. Oradell, NJ, Medical Economics Co, 1985. $19.95 (paperback)

Medical Practice Management. Third Edition. By Horace Cotton. 344 pp, illustrated. Oradell, NJ, Medical Economics Co, 1985. $28.50 (hardcover)

INTERNAL MEDICINE

Isler's Pocket Dictionary. A Guide to Disorders and Diagnostic Tests, Procedures, Terms. Second Edition. By Charlotte Isler, RN. 224 pp. Oradell, NJ, Medical Economics Co, 1985. $10.95 (paperback)

LEGAL MEDICINE

Legal Medicine 1985. Edited by Cyril H. Wecht, MD. 399 pp, illustrated. New York, NY, Praeger Publishers, 1985. $45.00 (hardcover)

MEDICAL HISTORY

Learning to Heal. The Development of American Medical Education. By Kenneth M. Ludmerer, MD. 368 pp. New York, NY, Basic Books Inc, 1985. $21.95 (hardcover)

MISCELLANEOUS

Tea with Demons. A True Story. The Perfect Wife. The Perfect Mother. The Perfect Daughter. The Perfect Professor. She could do it all until she went mad trying. By Carol Allen, PhD, Herbert S. Lustig, MD. 335 pp. New York, NY, William Morrow and Co, 1985. $17.95 (hardcover)

Diabetes. A New & Complete Guide to Healthier Living for Parents, Children & Young Adults Who Have Insulin-Dependent Diabetes. By Lee Ducat, Sherry Suib Cohen. 253 pp. New York, NY, Harper & Row Publishers, 1983. $7.95 (paperback)

Working With Backache. By Suzanne H. Rodgers, PhD. 179 pp, illustrated. Fairport, NY, Perinton Press, 1984. $18.95 (paperback)

The Brand-Name Nutrition Counter. By Jean Carper. 336 pp. New York, NY, Bantam Books, 1985. $3.95 (paperback)

State of the World, 1985. By Lester Brown, William U. Chandler, Christopher Flavin, et al. 301 pp, illustrated. New York, NY, W.W. Norton & Co, 1985. $8.95 (paperback)

Death of a Kaiser. By Jain I. Lin, MD. 125 pp. Dayton, OH, Landfall Press, Inc, 1985. $5.95 (paperback)

Change of Heart. The Bypass Experience. By Nancy Yanes Hoffman. 480 pp. New York, NY, Harcourt Brace Jovanovich, 1985. $17.95 (clothcover)

Your Personalized Health Profile: Choosing the Diet That's Right For You. By Myron Winick, MD. 263 pp, illustrated. New York, NY, William Morrow & Co, 1985. $16.95 (clothcover)

At Any Cost. Corporate Greed, Women, and the Dalkon Shield. By Morton Mintz. 308 pp. New York, NY, Pantheon Books, 1985. $17.95 (hardcover)

Healing the Wounds. A Physician Looks At His Work. By David Hilfiker, MD. 209 pp. New York, NY, Pantheon Books, 1985. $14.95 (hardcover)

The Healing Family. The Simonton Approach for Families Facing Illness. By Stephanie Matthews Simonton. 275 pp. New York, NY, Bantam Books, 1985. $3.95 (paperback)

The Rutgers Guide to Lowering Your Cholesterol. A Common-Sense Approach. By Hans Fisher, PhD, Eugene Boe. 218 pp. New Brunswick, NJ. Rutgers University Press, 1985. $16.95 (clothcover)

The Low Blood Sugar Cookbook. By Francyne Davis. 272 pp. New York, NY, Bantam Books, 1985. $3.95 (paperback)

NEPHROLOGY

Proteinuria. Edited by M.M. Avram, MD. 232 pp, illustrated. New York, NY, Plenum Publishing Corp, 1985. $35.00 (hardcover)

Contemporary Nephrology. Volume 3. Edited by Saulo Klahr, MD, Shaul G. Massry, MD. 768 pp, illustrated. New York, NY, Plenum Publishing Corp, 1985. $89.50 (hardcover)

OBSTETRICS AND GYNECOLOGY

Frontiers in Fertility. Edited by Betty Rothbard. 67 pp. New York, NY, Planned Parenthood of America, Inc, 1985. $8.95 (paperback)

ONCOLOGY

Monograph on Cancer Research No. 30. P-450 and Chemical Carcinogenesis. Edited by Yusaku Tagashira, Tsuneo Omura. 175 pp, illustrated. New York, NY, Plenum Publishing Corp, 1985. $49.50 (hardcover)

Medical Oncology. Basic Principles and Clinical Management of Cancer. Edited by Paul Calabresi, MD, Philip S. Schein, MD, Saul A. Rosenberg, MD. 1,400 pp, illustrated. New York, NY, MacMillan Publishing Co, 1985. $110.00 (hardcover)

Radiation Oncology. By Stewart M. Jackson, MD. 249 pp, illustrated. St. Louis, MO, Warren H. Green, Inc, 1985. $37.50 (hardcover)

PARASITOLOGY

Animal Agents and Vectors of Human Disease. Fifth Edition. Edited by Paul Chester Beaver, PhD, Rodney Clifton Jung, MD. 281 pp, illustrated. Philadelphia, PA, Lea & Febiger, 1985. $28.50 (hardcover)

PHARMACOLOGY

Guide to Parenteral Administration of Drugs. By C.E. Hipwell, M.L. Mashford, M.B. Robertson. 163 pp, illustrated. Easton, MD, Williams & Wilkins, 1984. $28.00 (hardcover)

The Pharmacological Basis of Therapeutics. Edited by Alfred Goodman Gilman, MD, Louis S. Goodman, MD, Theodore W. Rall, PhD, Ferid Murad, MD. 1,837 pp, illustrated. New York, NY, MacMillan Publishing Co, 1985. $65.00 (hardcover)

PSYCHIATRY

The New Psychiatry: How Modern Psychiatrists Think About Their Patients, Theories, Diagnosis, Drugs, Psychotherapies, Power, Training, Families, and Private Lives. By Jerrold S. Maxmen, MD. 329 pp. New York, NY, William Morrow & Co, 1985. $17.95 (softcover)

Study Guide and Self-Examination Review for Modern Synopsis of Comprehensive Textbook of Psychiatry/IV. Second Edition. By Harold I. Kaplan, MD, and Benjamin J. Sadock, MD. 551 pp, illustrated. Baltimore, MD, Williams & Wilkins, 1985. $22.95 (paperback)

Anger and Hostility In Cardiovascular and Behavioral Disorders. Edited by Margaret A. Chesney, PhD, Ray H. Rosenman, MD. 294 pp, illustrated. New York, NY, Hemisphere Publishing Corp, 1985. $39.95 (hardcover)

Human Sexuality: Psychosexual Effects of Disease. Edited by Martin Farber, MD. 335 pp, illustrated. New York, NY, Macmillan Publishing Co, 1985. $24.95 (paperback)

Stress and Anxiety. Volume 9. Edited by Charles D. Spielberger, Irwin G. Sarason, and Peter B. Defares. 283 pp, illustrated. New York, NY, Hemisphere Publishing Corp, 1985. $42.50 (hardcover)

Stress: Psychological and Physiological Interactions. Edited by Susan R. Burchfield. 399 pp, illustrated. New York, NY, Hemisphere Publishing Corp, 1985. $44.50 (hardcover)

Psychiatry: The State of the Art. Volume 5. Child and Adolescent Psychiatry, Mental Retardation, and Geriatric Psychiatry. Edited by P. Pichot, P. Berner, R. Wolf, K. Thau. 514 pp, illustrated. New York, NY, Plenum Publishing Corp, 1985. $55.00 (hardcover)

The Family, the Patient, and the Psychiatric Hospital: Toward a New Model. Formulated by the Committee on the Family Group for the Advancement of Psychiatry. 106 pp. New York, NY, Brunner/Mazel Publishers, 1985. $11.95 (softcover)

A DSM-III Casebook of Differential Therapeutics. A Clinical Guide to Treatment Selection. By Samuel Perry, MD, Allen Frances, MD, John Clarkin, MD. 392 pp. New York, NY, Brunner/Mazel Publishers, 1985. $37.50 (hardcover)

Lectures in Psychiatry. The Functional Psychoses: The Schizophrenias and Major Affective Disorders. By Ken Reed, MD, PhD. 292 pp, illustrated. St. Louis, MO, Warren H. Green, Inc, 1985. $37.50 (hardcover)

The Real Self. A Developmental, Self, and Object Relations Approach. Structure, Function, Development, Psychopathology, Treatment, Creativity. By James F. Masterson, MD. 192 pp. New York, NY, Brunner/Mazel Publishers, 1985. $25.00 (hardcover)

The Difficult Child. A New Step-by-Step Approach by a Noted Child Psychiatrist for Understanding and Managing Hard-to-Raise Children. By Stanley Turecki, MD, Leslie Tonner. 224 pp. New York, NY, Bantam Books, Inc, 1985. $15.95 (hardcover)

New Perspectives in Schizophrenia. Edited by Morton N. Menuck, MD, Mary V. Seeman, MD. 234 pp, illustrated. New York, NY, MacMillan Publishing Co, 1985. $29.95 (hardcover)

PUBLIC HEALTH

Double Exposure. Women's Health Hazards On The Job and At Home. Edited by Wendy Chavkin, MD. 276 pp, illustrated. New York, NY, Monthly Review Press, 1984. $10.00 (paperback)

Not In Our Backyards! Community Action for Health and the Environment. By Nicholas Freudenberg. 304 pp. New York, NY, Monthly Review Press, 1984. $10.00 (paperback)

RADIOLOGY

An Atlas of Critical Care Chest Roentgenography. By Lyle D. Victor, MD. 284 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1985. $45.00 (hardcover)

Magnetic Resonance of The Brain, Head and Neck. By William G. Bradley, Jr, MD, W. Ross Adey, MD, and Anton N. Hasso, MD. 130 pp, illustrated. Rockville, MD, Aspen System Corp, 1985. $65.00 (hardcover)

Essentials of Radiology Physics. By Charles A. Kelsey, PhD. 467 pp, illustrated. St. Louis, MO, Warren H. Green, Inc, 1985. $47.50 (hardcover)

SOCIAL TOPICS

Abortion Policy. An Evaluation of the Consequences for Maternal and Infant Health. By Jerome S. Legge, Jr. 182 pp, illustrated. Albany, New York, State University of New York Press, 1985. $34.50 (cloth)

Early Parenthood. Heaven or Hell. By Beverly Chalmers, PhD. 244 pp, illustrated. Juta & Co LTD. Kenwyn, Republic of So. Africa, 1984. $14.95 (paperback)

The Kids Next Door. Sons and Daughters Who Kill Their Parents. By Greggory W. Morris. 306 pp, New York, NY, William Morrow & Co, 1985. $16.96 (clothcover)

Social Controls and the Medical Profession. By Judith P. Swazey and Stephen R. Scher. 280 pp. Boston, MA, Oelgeschlager, Gunn & Hain, Inc, 1985. $27.50 (hardcover)

Social Organization of Medical Work. By Anselm Strauss, Shizuko Fagerhaugh, Barbara Suczek, and Carolyn Wiener. 310 pp. Chicago, IL. The University of Chicago Press, 1985. $25.00 (hardcover)

Abortion: Medical Progress and Social Implications. By Ciba Foundations Symposium 115. 285 pp, illustrated. London, Pitman Publishing Ltd, 1985. $27.95 (hardcover)

A Handbook of Social Science Methods. Quantitative Methods: Focused Survey Research and Causal Modeling. Volume 3. Edited by Robert B. Smith. 536 pp, illustrated. New York, NY, Praeger Publishers, 1985. $59.95 (hardcover)

The Physician and the Hopelessly Ill Patient. Legal, Medical and Ethical Guidelines. By The Society for the Right to Die. Edited by Sidney H. Wanzer, MD, et al. 98 pp, New York, NY, Society for the Right to Die, 1985. $5.00 (paperback)

SOFTWARE

Hypertension Management (Disk). By Edward P. Hoffer, MD, G. Octo Barnetts, MD. I.B.M. Disk, Easton, MD. Williams & Wilkins. $85.00 (disk)

SPORTS MEDICINE

Exercise and Sport Sciences Reviews. Volume 13, 1985. American College of Sports Series. Edited by Ronald L. Terjung, PhD. 596 pp, illustrated. New York, NY, Macmillan Publishing Co, 1985. $29.95 (hardcover)

TROPICAL MEDICINE

Essential Malariology. Second Edition. By Leonard Jan Bruce-Chwatt, MD. 452 pp, illustrated. London, William Heinemann Medical Books Ltd, 1985. $22.50 (hardcover)

UROLOGY

Urolithiasis and Related Clinical Research. Edited by Paul O. Schwille, Lynwood H. Smith, William G. Robertson, Winfried Vahlensieck. 997 pp, illustrated. New York, NY, Plenum Publishing Corp, 1985. $125.00 (hardcover)

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Frederick J. Briccetti, MD, Mount Kisco. Died September 5, 1985; age 62. He was a 1957 graduate of the Università Degli Studi di Bologna, Facoltà di Medicina e Chirurgia. Dr Briccetti was a Fellow of the American College of Gastroenterology and a Diplomate of the American Board of Internal Medicine. He was a member of the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Abraham Bohrer, MD, Forest Hills. Died August 19, 1985; age 84. Dr Bohrer was a 1928 graduate of New York Medical College, Flower and Fifth Avenue Hospital, New York. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Isaac B. Brodsky, MD, New York. Died September 17, 1985; age 89. Dr Brodsky was a 1921 graduate of New York Medical College, Flower and Fifth Avenue Hospital, New York. He was a member of the American Academy of Family Physicians, the Bronx County Medical Society and the Medical Society of the State of New York.

John Hilton Brown, MD, Peekskill. Died July 1, 1985; age 63. Dr Brown was a 1946 graduate of New York University College of Medicine. He was a member of the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Alexander R. Cowper, MD, Buffalo. Died July 28, 1985; age 67. He was a 1946 graduate of the University of Buffalo School of Medicine. Dr Cowper was a Diplomate of the American Board of Ophthalmology, and a member of the Academy of Medicine, the American Academy of Ophthalmology and Otolaryngology, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Joseph D'Agrosa, MD, Patchogue. Died September 9, 1985; age 60. He was a 1952 graduate of the State University of New York Downstate Medical Center. Dr D'Agrosa was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Suffolk County Medical Society and the Medical Society of the State of New York.

Enoch Victor Deutsch, MD, Great Neck. Died September 8, 1985; age 67. Dr Deutsch was a 1943 graduate of Middlesex University School of Medicine, Waltham. He was a Fellow of the American College of Anesthesiologists and a Diplomate of the American Board of Anesthesiology. His memberships included the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the Medical Society of the County of Kings and the Medical Society of the State of New York.

Howard Frank Drayer, MD, Watertown. Died August 24, 1985; age 87. Dr Drayer was a 1934 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a member of the American Psychiatric Association, the Medical Society of the County of Jefferson and the Medical Society of the State of New York.

Herman Freireich, MD, Flushing. Died April 9, 1985; age 73. He was a 1939 graduate of Università Degli Studi di Bologna, Facoltà di Medicina e Chirurgia. Dr Freireich was a Fellow of the American Academy of Family Physicians and a member of the American Geriatrics Society, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Milton Greenberg, MD, New Rochelle. Died August 3, 1985; age 82. He was a 1928 graduate of McGill University Faculty of Medicine, Montreal. Dr Greenberg was a member of the Aerospace Medical Association, the American Society of Tropical Medicine and Hygiene, the Bronx County Medical Association and the Medical Society of the State of New York.

Melvin J. Herman, MD, Bayside. Died September 24, 1985; age 63. He was a 1947 graduate of the Chicago Medical School. Dr Herman was a Fellow of the American Academy of Family Physicians and a Diplomate of the American Board of Family Practice. His memberships included the American Geriatrics Society, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Ernest Ludwig Hirsch, MD, Rego Park. Died September 17, 1985; age 91. Dr Hirsch was a 1922 graduate of the Universität Heidelberg Medizinische Fakultät, Baden. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Ada C. Hirsh, MD, New York. Died September 2, 1985; age 90. She was a 1936 graduate of Medizinische Fakultät der Universität, Wien. Dr Hirsh was a member of the American Psychiatric Association, the Academy of Psychoanalysis, the New York County Medical Society and the Medical Society of the State of New York.

Lucy Jaffe, MD, San Antonio, Texas. Died August 3, 1985; age 88. Dr Jaffe was a 1925 graduate of Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau. She was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Eva C. Rivka Kivelson, MD, New York. Died August 29, 1985; age 89. Dr Kivelson was a 1920 graduate of the Kiev Medical Institute. She was a member of

the New York County Medical Society and the Medical Society of the State of New York.

Rebecca G. Liswood, MD, Long Beach, California. Died December 24, 1984; age 88. Dr Liswood was a 1930 graduate of the New York Medical College, Flower and Fifth Avenue Hospital, New York. She was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

John J. Maddigan, MD, West Seneca. Died July 11, 1985; age 59. He was a 1951 graduate of Georgetown University School of Medicine. Dr Maddigan was a member of the Medical Society of the County of Erie and the Medical Society of the State of New York.

James Francis McGovern, MD, New York. Died September 10, 1985; age 62. Dr McGovern was a 1948 graduate of the State University of New York Downstate Medical Center. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Elmer Thomas McGroder, MD, Buffalo. Died August 13, 1985; age 88. He was a 1921 graduate of the University of Buffalo School of Medicine. Dr McGroder was a Fellow of the American College of Surgeons and a member of the Academy of Medicine, the Medical Society of the County of Erie and the Medical Society of the State of New York.

William James Nemon, MD, New York. Died December 8, 1984; age 45. Dr Nemon was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychiatric Association, the New York County Medical Society and the Medical Society of the State of New York.

Norman Nathan Ostrov, MD, New York. Died September 5, 1985; age 73. He was a 1939 graduate of Tufts University School of Medicine. Dr Ostrov was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Otolaryngology. His memberships included the Academy of Medicine, the American Academy of Otolaryngology, American Academy of Facial Plastic and Reconstructive Surgery, the American Broncho-Esophagological Association, the New York County Medical Society and the Medical Society of the State of New York.

C. James F. Parsons, MD, Bridgeport, Connecticut. Died September 2, 1985; age 87. Dr Parsons was a 1923 graduate of McGill University Faculty of Medicine, Montreal. He was a member of the Academy of Medicine, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Hyman Samuel Rosenfeld, MD, Garnerville. Died September 10, 1985; age 81. Dr Rosenfeld was a 1932 graduate of George Washington School of Medicine, Washington. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Barry Mayer Segal, MD, Briarcliff Manor. Died September 10, 1985; age 51. He was a 1959 graduate of the State University of New York Upstate Medical Center, Syracuse. Dr Segal was a Fellow of the American College of Physicians and the American College of Nuclear Medicine, and a Diplomate of the American Board of Internal Medicine and the American Board of Nuclear Medicine. His memberships included the Clinical Society of the New York Diabetes Association, the Endocrine Society, the Society of Nuclear Medicine, the American Thyroid Association, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

R. W. Sochynsky, MD, Brooklyn. Died September 17, 1985; age 69. Dr Sochynsky was a 1946 graduate of the Humboldt University Medical School, Berlin. Dr Sochynsky was a Fellow of the American Academy of Family Physicians and a member of the American Geriatrics Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

William Stark, MD, Floral Park. Died August 29, 1985; age 81. He was a 1928 graduate of the State University of New York Downstate Medical Center. Dr Stark was a qualified Fellow of the International College of Surgeons and a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Joseph Stein, MD, New York. Died September 6, 1985; age 83. Dr Stein was a 1928 graduate of New York University College of Medicine. He was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Bianca Steinhardt, MD, New York. Died July 3, 1985; age 93. Dr Steinhardt was a 1918 graduate of Medizinische Fakultät der Universität, Wien. She was a member of the New York County Medical Society and the Medical Society of the State of New York.

Thomas Kent Terrell, MD, Buffalo. Died July 24, 1985; age 62. He was a 1947 graduate of the University of Buffalo School of Medicine. Dr Terrell was a Fellow of the American College of Anesthesiologists and a Diplomate of the American Board of Anesthesiology. His memberships included the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the Medical Society of the County of Erie and the Medical Society of the State of New York.

Jay Richard Witten, MD, Brooklyn. Died July 27, 1985; age 42. He was a 1968 graduate of New York Medical College, Flower and Fifth Avenue Hospital, New York. Dr Witten was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Augustus Wolf, MD, New York. Died July 5, 1985; age 89. Dr Wolf was a 1918 graduate of Fordham University School of Medicine. He was a member of the Academy of Medicine, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Tamarath Knigin Yolles, MD, Stony Brook. Died July 29, 1985; age 66. Dr Yolles was a 1951 graduate of the New York University College of Medicine. She was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

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HOUSE OF DELEGATES

March 6 through 9, 1986
New York Hilton

SCHEDULE of SESSIONS

Thursday, March 6
Opening Session ..... 1:00 p.m.

Friday, March 7
Reference Committee Hearings ..... 8:30 a.m.–12:30 p.m.
Reference Committee Hearings ..... 1:30 p.m.–6:00 p.m.
Reference Committee Hearings ..... 8:00 p.m. (to completion)

Saturday, March 8
Second Session ..... 9:00 a.m.
Third Session ..... 1:30 p.m.

Sunday, March 9
Closing Session ..... 9:00 a.m.

A Guide to the 1986 Annual Meeting

Policy-making in The House of Delegates

This section of the New York State Journal of Medicine is a call to the officers, delegates, and members of the Medical Society of the State of New York to attend the 180th Annual Meeting of the Society and the meeting of its House of Delegates; 296 delegates representing 61 county medical societies, 9 district branches, specialty societies, the hospital medical staff section, 12 medical schools, the resident and medical student membership will meet at the Hilton Hotel in New York City on March 6–9, 1986.

The officers, members of the Council and the Board of Trustees, past presidents of the MSSNY, the Commissioner of the New York State Department of Health, and the Past President of the American Medical Association from New York, Gerald D. Dorman, MD, are also official representatives to the House.

Mandated by the Bylaws of the Society, this section lists the names of elected representatives, delegates who are serving on reference committees, and selections of the Nominating Committee for the election of Officers, Councilors, Trustees and AMA Delegates. Also included are the amendments to the Bylaws which will be considered by the House of Delegates.

Since the House of Delegates is the legislative body of the Society, charged with the general management of the State Society and its affairs, members of the Society are urged to use this information to consult with and advise their representatives. Resolutions introduced by the representatives bring members' concerns to the attention of the entire Society. Representatives not only have the responsibility to present the views of their constituents, but also to inform them of the actions taken by this governing body. The House of Delegates also formulates policy for the Society. No officer, councilor, board, commission, committee, or employee may initiate any policy unless such policy has been expressly approved by the House of Delegates or by the Council of the Society.

If one were to choose the most important work of the House of Delegates, it would have to be that of the reference committees. Any member of the Medical Society of the State of New York has the right to appear before any reference committee and participate in its deliberations. It is also in the reference committees that people outside of the State Society are asked to give their views. Nonmember physicians, guests or interested observers who wish to express their opinions may, with permission, come before the reference committee and speak to the business of the committee. I strongly urge members to use this forum to express their views.

Charles N. Aswad, MD, Speaker
House of Delegates

MEDICAL SOCIETY OF THE STATE OF NEW YORK

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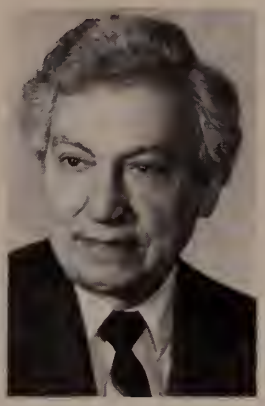

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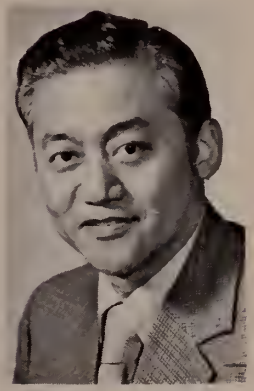

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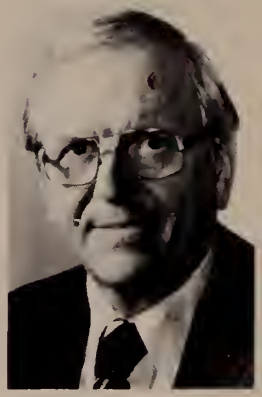
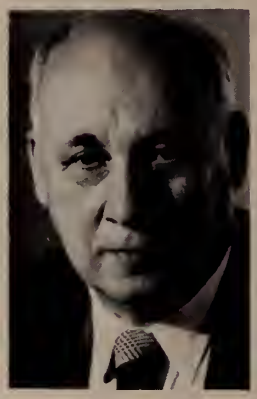
Joseph F. Shanaphy

Richmond



Victor J. Tofany

Monroe



Bernard J. Pisani

New York

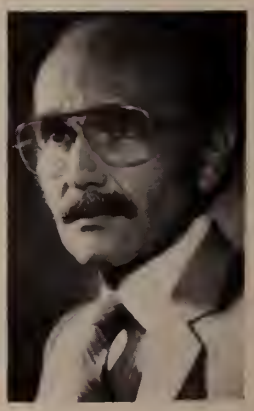
Councilors 1985–1986

Robert A. Mayers

Westchester

Thomas D. Pemrick

Rensselaer



Ralph E. Schlossman

Queens

Stanley A. Steckler

Suffolk

David M. Benford

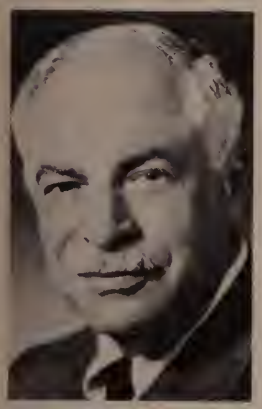
New York

Duane M. Cady

Onondaga

James M. Flanagan

Wayne



M. Theodore Tanenhaus

Kings

James H. Cosgriff, Jr.

Erie

Richard A. Hughes

Warren

Antonio F. LaSorte

Broome

Sydney Mishkin

Nassau

Robert J. Newborn
Albany
Medical Student

1986 HOUSE OF DELEGATES MEMBERS

The following is a list of members of the 1986 House of Delegates of the Medical Society of the State of New York.

Officers 1985–1986
President—Daniel F. O'Keeffe, Warren
President-Elect—John A. Finkbeiner, New York
Vice-President—Samuel M. Gelfand, Nassau
Secretary—John H. Carter, Albany
Assistant Secretary—George Lim, Oneida
Treasurer—Charles D. Sherman, Jr., Monroe
Assistant Treasurer—Morton M. Kurtz, Queens
Speaker—Charles N. Aswad, Broome
Vice-Speaker—Seymour R. Stall, Dutchess

Councilors
Term Expires 1986
Robert A. Mayers, Westchester
Thomas D. Pemrick, Rensselaer
Ralph E. Schlossman, Queens
Stanley A. Steckler, Suffolk

Term Expires 1987
David M. Benford, New York
Duane M. Cady, Onondaga
James M. Flanagan, Wayne
M. Theodore Tanenhaus, Kings

Term Expires 1988
James H. Cosgriff, Jr., Erie
Richard A. Hughes, Warren
Antonio F. LaSorte, Broome
Sidney Mishkin, Nassau

Student Councilor
Term Expires 1986
Robert J. Newborn, Albany

Resident Councilor
Term Expires 1986
Leon S. Serchuk, Queens

Trustees
G. Rehmi Denton, Albany, *Chairman*
Ralph M. Schwartz, Kings
Edgar P. Berry, New York
Richard D. Eberle, Onondaga
Joseph F. Shanaphy, Richmond
Victor J. Tofany, Monroe
Bernard J. Pisani, New York

Past Presidents
1959–1960—Henry I. Fineberg, Suffolk
1960–1961—Norman S. Moore, Tompkins
1961–1962—John M. Galbraith, Nassau
1966–1967—James M. Blake, Schenectady
1969–1970—Walter T. Heldmann, Richmond
1970–1971—Walter Scott Walls, Erie
1971–1972—George Himler, New York
1972–1973—Edward Siegel, Clinton
1974–1975—Lynn R. Callin, Monroe
1975–1976—Ralph S. Emerson, Nassau
1976–1977—George L. Collins, Jr., Erie
1977–1978—Carl Goldmark, Jr., New York
1978–1979—George T. C. Way, Dutchess
1979–1980—G. Rehmi Denton, Albany
1980–1981—Ralph M. Schwartz, Kings
1982–1983—Richard D. Eberle, Onondaga
1983–1984—Bernard J. Pisani, New York
1984–1985—Allison B. Landolt, Westchester

Past President of the American Medical Association
Gerald D. Dorman, New York

Vice-Speaker of the American Medical Association
John L. Clowe, Schenectady

Commissioner, New York State Department of Health

District Delegates
(*Elected Delegates of District Branches*)
First—Roger D. Billig, Richmond
Second—Robert Bruce Bergmann, Nassau
Third—Thomas W. Greenlees, Schoharie
Fourth—Michael J. Lynch, Washington
Fifth—Frederic A. Stone, Jefferson
Sixth—Vincent I. Maddi, Broome
Seventh—Verne M. Marshall, Ontario
Eighth—Robert James Reszel, Niagara
Ninth—Francis J. McMahon, Dutchess

Specialty Society Delegates
New York State Society of Anesthesiology—Edward C. Sinnott, Nassau
New York State Society of Dermatology—David Sibulkin, New York
New York Chapter American College of Emergency Physicians—Ralph Altman, New York
New York State Academy of Family Physicians—James R. Nunn, Erie
New York State Society of Internal Medicine—Robert M. Kohn, Erie
New York State Neurosurgical Society Inc.—Russel H. Patterson, Jr., New York
American College of Obstetricians and Gynecologists—District 11—Leonard S. Weiss, Orange
New York Occupational Medical Association, Inc.—Thomas J. Doyle, Queens
New York State Ophthalmological Society—Francis J. Gilroy, Broome

New York State Society of Orthopaedic Surgeons, Inc.—Leo Arthur Green, Queens
New York State Society of Otolaryngology—Head and Neck Surgery—Anthony J. Durante, Nassau
New York State Society of Pathologists—Edward C. Zaino, Nassau
American Academy of Pediatrics—District 11—Marvin L. Blumberg, Queens
New York Society of Physical Medicine and Rehabilitation, Inc.—David Ernstoff, Queens
New York Regional Society of Plastic and Reconstructive Surgery—Philip C. Bonanno, Westchester
New York State Psychiatric Association—Harold E. Berson, Kings
New York State Chapter—American College of Radiology —Victor A. Panaro, Erie
New York State Society of Surgeons, Inc.—Theodore C. Max, Oneida
New York State Urological Society, Inc.—Lawrence Ravich, Nassau

Delegates from Component County Medical Societies

Albany (*4*)
John W. Abbuhl, Albany
William O'Dwyer, Latham
James H. Puleo, Albany
Nathan P. Reed, Albany

Allegany (*1*)
Gary W. Ogden, Andover

Bronx (*10*)
John P. Albanese, Bronx
Marcos A. Charles, Bronx
Dattatraya G. Lanjewar, Pelham Manor
Charles Laverdi, Bronx
Stanley Luftschein, Bronx
Hugo M. Morales, Bronx
Govindappa Rangaiah, Scarsdale
Howard S. Schwartz, Bronx
Tullio F. Tartaglia, Bronx
Juana Toporovsky, Bronx

Broome (*4*)
Louis W. Giordano, Endicott
Theodore R. Poritz, Binghamton
Jeffrey A. Ribner, Binghamton
Irwin J. Rosenberg, Endicott

Cattaraugus (*1*)
Adil Husain Al-Humadi, Olean

Cayuga (*1*)
Richard J. Freeman, Auburn

Chautauqua (*2*)
James G. Dahlie, Jamestown
Charles R. Sinatra, Jamestown

Chemung (*2*)
Donald L. Brooks, Jr., Elmira
Gerald P. Schneider, Elmira

Chenango (*1*)
Norman C. Lyster, Jr., Norwich

Clinton (*1*)
Robert T. Potter, Plattsburgh

Columbia (*1*)
Rosewell D. Shaw, Stottville

Cortland (*1*)

Delaware (*1*)
Gary Preiser, Walton

Dutchess (*4*)
Eric B. Brocks, Fishkill
Stephen R. Chernay, Fishkill
Eleanor C. Kane, Poughkeepsie
Arthur W. Menken, Poughkeepsie

Erie (*9*)
Victorino Anllo, Amherst
Thomas W. Bradley, Kenmore
Robert A. Caputi, Buffalo
Anthony J. Federico, Buffalo
Allen L. Lesswing, Snyder
Milford C. Maloney, Buffalo
Leo E. Manning, Amherst
James F. Phillips, Jr., Buffalo
Joseph A. Prezio, Buffalo

Essex (*1*)

Franklin (*1*)
Alfred A. Hartmann, Sr., Malone

Fulton (*1*)
Armand J. D'Errico, Gloversville

Genesee (*1*)
Alfred L. George, Batavia

Greene (*1*)
Karuvath Enu, Hudson

Herkimer (*1*)
Krishna K. Vadlamudi, Ilion

Jefferson (*2*)
William Bruce Carter, Watertown
David O. VanEenenaam, Watertown

Kings (*19*)
Grace A. Altenau, Brooklyn
Lawrence Ames, Brooklyn
Norman S. Blackman, Brooklyn
Randall D. Bloomfield, Brooklyn
Joseph R. Brennan, Brooklyn
George W. Calvosa, Brooklyn
Vernal G. Cave, Brooklyn
Duncan W. Clark, Brooklyn
Paul Finkelstein, Brooklyn
Stanley I. Fishman, Massapequa
Robert E. Gordon, Brooklyn

Ladislav P. Hinterbuchner, Brooklyn
A. W. Martin Marino, Jr., Brooklyn
Martin Markowitz, Brooklyn
Bentley D. Merrim, Brooklyn
Hubert S. Pearlman, Brooklyn
Leon Morton Rothman, New York City
Harold N. Schwinger, Roslyn
Leo J. Swirsky, Brooklyn

Lewis (*1*)
John C. Herrman, Lowville

Livingston (*1*)
Sheppard Arluck, Geneseo

Madison (*1*)
Leonard A. Argentine, Oneida

Monroe (*7*)
William A. Dolan, Rochester
Warren Glaser, Rochester
William A. Kern, Jr., Rochester
Vito P. Laglia, Rochester
Mario B. LoMonaco, Rochester
Joyce M. McChesney, Rochester
Charles R. Salamone, Rochester

Montgomery (*1*)

Nassau (*11*)
Lee S. Binder, Valley Stream
Morton Goldfarb, Massapequa Park
Jeffrey Theodore Kessler, Great Neck
Paul C. Lehmuller, Levittown
Arnold D. Lurie, Baldwin
Alfred W. Marks, Rockville Centre
Felix A. Monaco, Rockville Centre
John A. Ostuni, Freeport
Neal A. Sckolnick, Rockville Centre
Arthur J. Wise, Jr., Manhasset
Jerome Zwanger, Massapequa

New York (*23*)
Arnold L. Bachman, New York City
Melvin H. Becker, Manhasset
Robert S. Bernstein, New York City
Irwin J. Cohen, New York City
Hugh Clark Davidson, New York City
Wilbur J. Gould, New York City
Michael H. Grieco, New York City
George Hyams, New York City
Virginia Kanick, New York City
Vance Lauderdale, Jr., New York City
Samuel H. Madell, New York City
Aaron G. Meislin, New York City
George W. Melcher, Jr., New York City
Richard B. Nolan, New York City
Donna B. O'Hare, New York City
Stuart I. Orsher, New York City
Richard N. Pierson, Jr., New York City
William B. Rawls, Pleasant Valley
Isadore Rosenfeld, New York City
Albert M. Schwartz, New York City
Miriam Z. Seborer, New York City
Clifford L. Spingarn, New York City
Meyer Texon, New York City

Niagara (*3*)
Claus Michael Fichte, Niagara Falls
James J. Kropelin, Niagara Falls
Harry Thomas Oliver, Newfane

Oneida (*3*)
Gerald C. Gant, New Hartford
Robert M. George, Utica
Neville W. Harper, Rome

Onondaga (*6*)
Daniel L. Dombroski, Syracuse
John A. Hoepner, Syracuse
Richard A. Konys, Syracuse
Arthur Lehrman, Syracuse
Frank J. Piper, Syracuse
George P. Tilley, Syracuse

Ontario (*2*)
Thomas A. McCormick, Geneva
Kenneth T. Steadman, Geneva

Orange (*4*)
Stanley F. Brunn, Port Jervis
Stanley L. Grossman, Newburgh
Jack Manpel, New Windsor
Ansel R. Marks, Middletown

Orleans (*1*)
David B. L. Meza, III, Albion

Oswego (*1*)
Kathaleen C. Perkins, Oswego

Otsego (*1*)
Rodman D. Carter, Cooperstown

Putnam (*1*)
Hari P. Chakravorty, Mahopac

Queens (*16*)
Jugal K. Agrawal, Flushing
Daniel M. Chansky, Forest Hills
John W. V. Cordice, Jr., St. Albans
Alexander M. De la Garza, Flushing
Robert M. Farrell, Flushing
Fred N. Flatau, Flushing
Irving G. Frohman, Rockaway Beach
Victor Guarneri, Bayside
Edith Gutman, Beechhurst
Nicetas H. Kuo, Great Neck
Maxwell Jerome Marder, Forest Hills
Hilda Ratner, Beechhurst
Nessim J. Romano, Forest Hills
Sheldon D. Sax, Whitestone
Ezra A. Wolff, Manhasset

Rensselaer (*2*)
William M. McCarty, Troy
William A. Whyland, Troy

Richmond (*3*)
B. Basil Hyman, Staten Island
Gerald J. Lustig, Staten Island
Robert J. Slich, Staten Island

Rockland (*4*)
Herbert Z. Geller, New City
Michael A. Kalvert, Bardonia
Roy H. Lieberman, Nanuet
Stanley H. Oransky, Bardonia

St. Lawrence (*1*)
Henry Joseph Dobies, Massena

Saratoga (*1*)

Schenectady (*3*)
Richard H. Lange, Schenectady
John M. Spring, Schenectady
Donald Wexler, Schenectady

Schoharie (*1*)
Frederick J. Michel, Cobleskill

Schuyler (*1*)
Cynthia Sue Terry, Montour Falls

Seneca (*1*)
Donald W. Bidwell, Seneca Falls

Steuben (*2*)
Jack D. O'Neil, Corning
Wayne C. Templer, Corning

Suffolk (*11*)
William H. Bloom, Bay Shore
Stephen I. Braitman, Islip Terrace
Clive D. Caplan, Islip Terrace
Frank R. Collier, Port Jefferson
John G. Egner, West Islip
Robert E. Fear, Southampton
James A. Holleran, East Setauket
Elise H. Korman, Southampton
Phillip I. Levitan, Smithtown
Nathaniel B. Messinger, Islip Terrace
Melvin Shuter, Islip Terrace

Sullivan (*1*)
Seymour Cohen, Monticello

Tioga (*1*)

Tompkins (*2*)

Ulster (*2*)
Joseph B. Basile, Kingston
Geraldine T. Keyes, Kingston

Warren (*2*)
Franklin A. DePeters, Glens Falls
Robert A. Reid, Glens Falls

Washington (*1*)
Arnold B. Wise, Cambridge

Wayne (*1*)
Norman R. Loomis, Ontario

Westchester (*9*)
Ann Cea, Rye Brook
Richard L. Fenton, Tarrytown
Armond V. Mascia, Tarrytown
Stanley M. Mendelowitz, Tarrytown
Richard L. Petrillo, Mount Vernon
John A. Ramsdell, White Plains
Thomas Dignan Rizzo, Bronxville
Michael Sierp, Yonkers
William J. Walsh, Jr., White Plains

Wyoming (*1*)
John Thomas Reagan, Perry

Yates (*1*)
Michael J. Boquard, Penn Yan

Medical School Delegates-12
Albany Medical College of Union University—Samuel Steven Ciccio, Albany
Albert Einstein College of Medicine—Melvin Nat Zelefsky, Bronx
Columbia University College of Physicians and Surgeons—Linda D. Lewis, New York
Cornell University Medical College—Jack Richard, New York
Mount Sinai School of Medicine of City University of New York—David Adolph Dreiling, New York
New York Medical College—Michael L. Friedland, Westchester
New York University School of Medicine—Stanford Wessler, New York
State University of New York at Buffalo School of Medicine—Charles Wilburn Pruet, Erie
State University of New York Downstate Medical Center—
State University of New York at Stony Brook School of Medicine—Dorothy Spiegel Lane, Suffolk
State University of New York Upstate Medical Center in Syracuse—Kenneth S. K. Ho, Onodaga
University of Rochester School of Medicine and Dentistry—Thomas E. Cardillo, Monroe

Medical Student Delegates (3)

Resident Membership Delegate (1)
John Francis Madden, Westchester

Hospital Medical Staff Delegate (1)
Richard John Dwane, Cayuga

REFERENCE COMMITTEES

Reports of Officers and Administrative Matters

Stanley F. Brunn, Orange, *Chairman*
Frank R. Collier, Suffolk
Gerald J. Lustig, Richmond
John A. Ramsdell, Westchester
John M. Spring, Schenectady

ANNUAL REPORTS REFERRED TO COMMITTEE:
President
President-Elect
Secretary
Treasurer
Board of Trustees
Budget and Finance
Executive Vice-President
New York Delegation to the AMA
District Branches
Physicians' Home
Search Committee for the Position of Executive Vice-President
Long-Range Planning
Administrative Committee for the MSSNY Pension Program
New York State Society of Medical Assistants, Inc., Advisory Committee to
Foreign Medical Graduates
General Insurance
Membership Programs
Publications, Library, and Archives
Résumé of Instructions from the 1985 House of Delegates Ad Hoc Committee to Study the Feasibility of Relocating MSSNY Headquarters

Bylaws

James R. Nunn, NYS Academy of Family Physicians, *Chairman*
Sheppard Arluck, Livingston
Randall D. Bloomfield, Kings
Eleanor C. Kane, Dutchess
Stanley Luftschein, The Bronx

ANNUAL REPORT REFERRED TO COMMITTEE:
Résumé of Instructions from the 1985 House of Delegates

Public Health and Education

Nicetas H. Kuo, Queens, *Chairman*
Michael L. Friedland, New York Medical College
John A. Ostuni, Nassau
Richard L. Pierson, Jr., New York
Charles R. Salamone, Monroe

ANNUAL REPORTS REFERRED TO COMMITTEE:
Accident and Injury Prevention
Aging and Nursing Homes
Alcoholism
Cancer
Child Abuse
Drug Abuse
Emergency Medical Services
Environmental Quality
Home Health Care and Hospice
Maternal and Child Health
Mental Health
Physical Medicine and Rehabilitation
Physicians' Health
Preventive Medicine
School Health and Sports Medicine
Continuing Medical Education
Forensic Medicine
Information Technology in Medicine
Medical School Relations
Scientific Program
Résumé of Instructions from the 1985 House of Delegates Ad Hoc Committee on Bioethical Issues

Governmental Affairs and Legal Matters

David B. L. Meza, III, Orleans, *Chairman*
Roger D. Billig, First District
Clive D. Caplan, Suffolk
Arthur W. Menken, Dutchess
Jeffrey A. Ribner, Broome

ANNUAL REPORTS REFERRED TO COMMITTEE:
Ethics
Judicial Council
Legislation
HANYS/MSSNY Liaison Committee
New York State Association of the Professions
Professional Medical Liability Insurance and Defense Board
Résumé of Instructions from the 1985 House of Delegates Ad Hoc Committee on the Conduct of OPMC Investigations

Medical Services

Hugh Clark Davidson, New York, *Chairman*
Dattatraya G. Lanjewar, The Bronx
Linda D. Lewis, Columbia University College of Physicians and Surgeons
Milford C. Maloney, Erie
Stanley H. Oransky, Rockland

ANNUAL REPORTS REFERRED TO COMMITTEE:
Alternative Health Care Delivery Systems
Health Planning
Hospital and Professional Relations
Interspecialty
Medicaid
Medical Care Insurance
Social Security Administration Disability Benefits Program, Committee to Monitor and Provide Input Into
Workers' Compensation and Occupational Health
Résumé of Instructions from the 1985 House of Delegates

CONVENTION COMMITTEES

Credentials

A. W. Martin Marino, Jr., Kings, *Chairman*
Fred N. Flatau, Queens
Vincent I. Maddi, Sixth District
Theodore C. Max, New York State Society of Surgeons
Joyce M. McChesney, Monroe

Rules and Order of Business

Rodman D. Carter, Otsego, *Chairman*
Robert E. Gordon, Kings
Wilbur J. Gould, New York
Lawrence Ravich, New York State Urological Society
Nathan P. Reed, Albany

Sergeant at Arms

John C. Hermann, Lewis, *Chairman*
Ann Cea, Westchester
Henry Joseph Dobies, St. Lawrence
Felix A. Monaco, Nassau
James F. Phillips, Erie

Tellers

Richard H. Lange, Schenectady, *Chairman*
Richard John Dwane, Hospital Medical Staff Section
Elise H. Korman, Suffolk
Robert James Reszel, Eighth District
Miriam Z. Seborer, New York

NOMINATING COMMITTEE

To the House of Delegates, Ladies and Gentlemen:

In accordance with Article XI, Section 2 of the Bylaws of the Medical Society of the State of New York, the Nominating Committee met at the Society's headquarters, 420 Lakeville Road, Lake Success, New York, on Thursday, October 3, 1985, at 10:30 a.m.

Members of the committee present were:
Member-at-Large—**Allison B. Landolt, M.D.**, Westchester, *Chairman*
First District Branch—**David M. Benford, M.D.**, New York
Second District Branch—**Stanley A. Steckler, M.D.**, Suffolk
Third District Branch—**Thomas D. Pemrick, M.D.**, Rensselaer
Fourth District Branch—**Franklin A. DePeters, M.D.**, Warren
Fifth District Branch—**Robert M. George, M.D.**, Oneida
Sixth District Branch—**Irwin J. Rosenberg, M.D.**, Broome
Seventh District Branch—**James M. Flanagan, M.D.**, Wayne
Eighth District Branch—**Bruce E. Baker, M.D.**, Genesee
Ninth District Branch—**Seymour R. Stall, M.D.**, Dutchess
Member-at-Large—**Victor J. Tofany, M.D.**, Monroe

After careful consideration of the recommendations submitted by the district branches and the county medical societies in response to a memorandum dated July 18, 1985, and nominations from the floor, your committee respectfully nominated the following candidates for election on March 9, 1986:

President—**John A. Finkbeiner, M.D.**, New York
President-Elect—**Samuel M. Gelfand, M.D.**, Nassau
Vice-President—**Charles D. Sherman, Jr., M.D.**, Monroe
Secretary—**John H. Carter, M.D.**, Albany
Assistant Secretary—**George Lim, M.D.**, Oneida
Treasurer—**Morton Kurtz, M.D.**, Queens
Assistant Treasurer—**Robert A. Mayers, M.D.**, Westchester
Speaker—**Charles N. Aswad, M.D.**, Broome
Vice-Speaker—**Seymour R. Stall, M.D.**, Dutchess
Trustees (one for five years)—**Daniel F. O'Keeffe, M.D.**, Warren
Councilors (four for three years)—**Robert E. Fear, M.D.**, Suffolk
Stanley L. Grossman, M.D., Orange
Thomas D. Pemrick, M.D., Rensselaer
Ralph E. Schlossman, M.D., Queens
Student Councilor (one for one year)—**Frances Hartenstein**, Monroe
Resident Councilor (one for one year)—

Delegates to the American Medical Association for two years commencing January 1, 1987:
Charles N. Aswad, M.D., Broome
Edgar P. Berry, M.D., New York
John L. Clowe, M.D., Schenectady
Hugh Clark Davidson, M.D., New York
William A. Dolan, M.D., Monroe
Richard D. Eberle, M.D., Onondaga
Robert E. Fear, M.D., Suffolk
Robert E. Gordon, M.D., Kings
James J. Kropelin, M.D., Niagara
Dattatraya G. Lanjewar, M.D., The Bronx
Samuel H. Madell, M.D., New York
Robert A. Mayers, M.D., Westchester
Richard N. Pierson, Jr., M.D., New York
Joseph A. Prezio, M.D., Erie
Irwin J. Rosenberg, M.D., Broome
Charles R. Salamone, M.D., Monroe
Ralph M. Schwartz, M.D., Kings
Joseph F. Shanaphy, M.D., Richmond
Stanley A. Steckler, M.D., Suffolk
George T. C. Way, M.D., Dutchess

The ten nominees receiving the largest number of votes will be delegates; the second ten will be alternates.

Allison B. Landolt, M.D., *Chairman*

HOUSE COMMITTEE ON BYLAWS

To the House of Delegates, Ladies and Gentlemen:

The members of the House Committee on Bylaws are as follows:

George Lim, M.D., Chairman ..... Oneida
Stanley F. Brunn, M.D. ..... Orange
Rodman D. Carter, M.D. ..... Otsego
Robert M. Kohn, M.D. ..... Erie
Sidney L. Mishkin, M.D. ..... Nassau
James R. Nunn, M.D. ..... Erie
Donna B. O'Hare, M.D. ..... New York
Hilda Ratner, M.D. ..... Queens
Stanley A. Steckler, M.D. ..... Suffolk
Daniel F. O'Keeffe, M.D. President, ex officio .. Warren
John H. Carter, M.D., Secretary, ex officio ... Albany
Charles N. Aswad, M.D., Speaker, ex officio . Broome
George J. Lawrence, Jr., M.D., Executive Vice President, ex officio ..... Queens
Donald R. Moy, J.D., ... General Counsel, ex officio

A meeting of the Reference Committee on Bylaws was held at the Hilton Hotel in New York City on June 7, 1985. The Reference Committee prepared a transcript of testimony and a summary of its recommendations to the House Committee on Bylaws. The input received from the meeting of the Reference Committee on Bylaws proved to be of great assistance to the House Committee on Bylaws when it met on September 26, 1985.

In all, five resolutions, asking for amendments to the Bylaws, were referred to the Committee for its consideration.

The following actions were taken with respect to the resolutions referred to the Committee:

Resolution 85-2, Sharing Delegates Expenses

Introduced by Medical Society of the County of Erie, Inc.

Whereas, The Medical Society of the State of New York has held almost every annual meeting of the House of Delegates in New York City during the past twenty years; and

Whereas, The cost of meals, taxis and hotels in New York City is now double the amounts charged in Upstate metropolitan centers; and

Whereas, The Upstate county medical societies have received no relief from this outrageous financial burden year after year (now about $1,000 per delegate); and

Whereas, The delegates themselves have had no relief from the personal sacrifice of longer traveling time, absence from family and family affairs, absence from hospital and office patient contacts in comparison to their colleagues downstate; and

Whereas, On January 10, 1985, the Council took action to continue to hold the House of Delegates meetings in New York City in the future; therefore be it

Resolved, That Article XVI, of the Bylaws of the Medical Society of the State of New York be amended by the addition of the following paragraph between paragraphs four and five: (additions italicized)

Delegates of the component county medical societies affiliated with the State Society shall be allowed necessary expenses to attend meetings of the House of Delegates on a dollar-for-dollar matching basis with the component county medical societies to an amount not to exceed fifty percent of the allowance approved by the Board of Trustees for those delegates whose total expenses are now reimbursed by the Medical Society of the State of New York.

Fiscal Note: 204 County delegates @ $950 $193,800

50% MSSNY's share $96,900
50% CMSs' share $96,900

The House Committee on Bylaws polled all county medical societies regarding the financial support they provide to their delegates who attend the Annual Meeting of the MSSNY House of Delegates. While the level of support varies county by county, the poll indicated that the average cost per delegate per day is $200. After considerate discussion, the committee agreed that a reimbursement of $100 per day is reasonable because it represents a reimbursement of approximately one half of the costs incurred by each delegate. The House Committee on Bylaws, therefore, proposes the following substitute resolution for Resolution 85-2:

Resolved, That Article XVI of the Bylaws of the Medical Society of the State of New York be amended by the addition of the following paragraph between paragraphs four and five: (additions italicized)

"Delegates of the component county medical societies of the Medical Society of the State of New York and specialty society delegates shall be reimbursed by the State Society with a per diem allowance of not less than $100 per day for each day the House is in session, if the delegate is registered at a hotel while attending the convention. The Council, with the approval of the Board of Trustees, shall determine the per diem allowance on an annual basis.

FISCAL NOTE — Based upon the current number of county medical society and specialty society delegates, the minimum annual cost to the State Society is $89,200.

It should be noted that pursuant to the above reimbursement formula, specialty societies having delegates at the Annual Meeting will receive reimbursement on the same basis as component county medical societies. There will be no reimbursement for alternate delegates.

The House Committee on Bylaws, therefore, recommends **APPROVAL** of the substitute resolution for Resolution 85-2.

Resolution 85-20, Speaker to be a Member of the Executive Committee

Introduced by Medical Society of the County of Westchester, Inc.

Whereas, The Speaker, by virtue of his office presides at all meetings of the House of Delegates which is the governing body of the Medical Society of the State of New York; and

Whereas, The Council exercises all the rights and duties of the House of Delegates when the House of Delegates is not in session; and

Whereas, The Council is in fact the Executive Committee of the House of Delegates; and

Whereas, The Executive Committee of the Council has the authority to take emergency action between Council meetings; therefore be it

Resolved, That the Bylaws of the Medical Society of the State of New York be amended to allow the Speaker to be a member of the Executive Committee; and be it further

Resolved, That Article IV, Section 4, paragraph 1 of the Bylaws of the Medical Society of the State of New York be amended by adding the words "The Speaker." Article IV, Section 4, paragraph 1 would then read: (additions italicized)

The Council shall establish an executive committee to be composed of the president, the vice-president, the president-elect, the immediate past-president, the secretary, the treasurer, *the speaker*, the chairman of the Board of Trustees, and two additional members of the Council appointed by the president with the approval of the Council.

and be it further

Resolved, That Article V, Section 2, paragraph 1 under the heading, "Speaker," of the Bylaws be amended by adding a new sentence after the first sentence, to read:

"He shall serve on the executive committee."

Article V, Section 2, paragraph 1 under the heading "Speaker" would then read: (additions italicized)

"The speaker shall preside at all meetings of the House of Delegates. *He shall serve on the executive committee.* He shall appoint all committees to serve during the meeting of the House of Delegates at least thirty days in advance of the meeting. All resolutions submitted by component county medical societies, district branches, scientific sections, and medical schools to be presented to the House of Delegates should be forwarded to the speaker at least forty-five days in advance of the annual meeting of the House and referred by him to the appropriate reference committees; and all resolutions sent in subsequent to forty-five days should be presented to the House and referred to the appropriate reference committees."

and

Resolution 85-41, The Speaker as a Member of the Executive Committee

Introduced by Allison B. Landolt, M.D., Daniel F. O'Keeffe, M.D. and John A. Finkbeiner, M.D., as Individuals

Resolved, That the Speaker of the House of Delegates of the Medical Society of the State of New York shall serve on the Executive Committee of the Council; and be it further

Resolved, That Article IV, Section 4, paragraph 1 of the Bylaws of the Medical Society of the State of New York be amended to read as follows: (additions italicized)

The Council shall establish an executive committee to be composed of the president, the vice-president, the president-elect, the immediate past-president, the secretary, the treasurer, *the speaker*, the Chairman of the Board of Trustees, and two additional members of the Council appointed by the president with the approval of the Council.

and be it further

Resolved, That Article V, Section 2, paragraph 1, under the heading "Speaker," of the Bylaws be amended by adding a new sentence after the first sentence, to read:

"He shall serve on the executive committee."

Article V, Section 2, paragraph 1 under the heading "Speaker," would then read: (additions italicized)

"The speaker shall preside at all meetings of the House of Delegates. *He shall serve on the executive committee.* He shall appoint all committees to serve during the meeting of the House of Delegates at least thirty days in advance of the meeting. All resolutions submitted by component county medical societies, district branches, scientific sections, and medical schools to be presented to the House of Delegates should be forwarded to the speaker at least forty-five days in advance of the annual meeting of the House and referred by him to the appropriate reference committees; and all resolutions sent in subsequent to forty-five days should be presented to the House and referred to the appropriate reference committees.

Because of the similarity of content, the committee reviewed Resolutions 85-20 and 85-41 at the same time. The committee is in agreement with these resolutions and feels that it is essential for the Speaker to have an active role in the deliberations of the Executive Committee of the State Society.

The House Committee on Bylaws, therefore, recommends **APPROVAL** of Resolutions 85-20 and 85-41.

Resolution 85-44, Representation in MSSNY Hospital Medical Staff Section

Introduced by Richard J. Dwane, M.D., Hospital Medical Staff Section Delegate

Whereas, Membership in the hospital medical staff section of the Medical Society of the State of New York is currently limited to representatives of the medical staffs of acute care hospitals in New York State; and

Whereas, There exists no definition of the term "acute care hospital" under New York State law; and

Whereas, Members of the MSSNY on the staffs of psychiatric and other non-acute care hospitals share many of the same concerns with members who are on the medical staffs of acute care general hospitals, and should have the same right of representation within the Hospital Medical Staff Section; and

Whereas, The hospital medical staff section of the American Medical Association extends membership to representatives of all hospitals' medical staffs; therefore be it

Resolved, That representation in the hospital medical staff section of the Medical Society of the State of New York be extended to include the elected representatives of medical staffs of hospitals licensed under the Mental Hygiene Law of New York State as well as of any other hospital with a minimum of 35 beds which is located in New York State; and be it further

Resolved, That paragraph 1 of Article XII-A of the Bylaws of the Medical Society of the State of New York be amended as follows: (additions italicized)

The hospital medical staff section is authorized to be represented in the House of Delegates by 1 delegate. The hospital medical staff section shall represent physicians on the medical staffs of acute care hospitals located in New York State, *of hospitals licensed under the Mental Hygiene Law of New York State, and of any other hospital in the State of New York with a minimum of 35 beds.*

The term "acute care" has been interpreted to mean general hospitals under the Public Health Law. This interpretation excludes representation of various psychiatric hospitals under the jurisdiction of the Office of Mental Health or psychiatric hospitals maintained directly by the State of New York or its political subdivisions. Because these facilities maintain inpatient psychiatric services, including psychiatric services of an acute nature, the House Committee on Bylaws believes that the Bylaws should be clarified to provide representation of hospitals with inpatient programs certified by the New York State Office of Mental Health and psychiatric inpatient facilities maintained by the State of New York or its political subdivisions.

The Committee, therefore proposes the following substitute resolution for Resolution 85-44:

Resolved—That paragraph 1 of Article XII-A of the Bylaws of the Medical Society of the State of New York be amended as follows: (additions italicized)

The hospital medical staff section is authorized to be represented in the House of Delegates by 1 delegate. The hospital medical staff section shall represent physicians on the medical staffs of acute care hospitals located in New York State; *of psychiatric inpatient facilities maintained by the State of New York or its political subdivisions; and of hospitals with inpatient programs certified by the New York State Office of Mental Health.*

The Committee believes that the substitute resolution more clearly identifies those hospitals represented by the hospital medical staff section.

The House Committee on Bylaws, therefore, recommends **APPROVAL** of the substitute resolution for Resolution 85-44.

Resolution 85-62, Introduction of Resolutions

Introduced by: John L. Clowe, M.D., as an Individual

Whereas, The Bylaws of the Medical Society of the State of New York stipulate that all resolutions to be presented to the House of Delegates should be forwarded to the speaker at least forty-five days in advance of the annual meeting of the House; and

Whereas, The Bylaws further stipulate that no new resolutions shall be introduced at the last scheduled session except by a unanimous vote of the House of Delegates; and

Whereas, The 1975 House of Delegates mandated that resolutions must be in the headquarters office thirty days before the opening of the House of Delegates; and

Whereas, The present deadline for introducing resolutions is unmanageable, and the requirement of a unanimous vote for acceptance of late resolutions is too restrictive; therefore be it

Resolved, That Article V, Section 2, the paragraph entitled "Speaker" be amended to read as follows: (additions italicized, deletions in brackets)

The speaker shall preside at all meetings of the House of Delegates. He shall appoint all committees to serve during the meeting of the House of Delegates at least thirty days in advance of the meeting. All resolutions submitted by *members of the House of Delegates* (*pursuant to Article III, Section 3, paragraph 3*) [component county medical societies, district branches, scientific sections, and medical schools] to be presented to the House of Delegates should* be forwarded to the speaker at least [forty-five] *thirty* days in advance of the annual meeting of the House of Delegates and referred by him to the appropriate reference committees; [and all resolutions sent in subsequent to forty-five days should be presented to the House and referred to the appropriate reference committees;] and be it further

Resolved, That Article III, Section 3, paragraph 4 of the Bylaws be amended to read as follows: (deletions in brackets, additions italicized)

[No new resolutions shall be introduced at the last scheduled session except by a unanimous vote of the House of Delegates.]

Resolutions to be presented to the House of Delegates should be forwarded to the speaker at least thirty days in advance of the annual meeting of the House of Delegates. Resolutions may be presented by a voting delegate any time prior to the final day of the annual meeting of the House of Delegates but will be accepted for consideration by the House of Delegates only upon ⅔ vote of delegates present and voting.*

Resolutions of an emergency nature presented by voting delegates on the final day of the annual meeting of the House of Delegates shall be referred by the speaker to an appropriate reference committee, which shall then report to the House as to whether the matter involved is or is not of an emergency nature.

If the reference committee reports that the matter is of an emergency nature, it shall be presented to the House without further consideration by a reference committee. Favorable action shall require the affirmative vote of ¾ of all delegates present and voting. If the reference committee reports that the matter is not of an emergency nature, the speaker shall defer its introduction until the next annual meeting of the House of Delegates.

The House Committee on Bylaws, after thorough deliberation, agrees that the above method more clearly defines the procedures to be followed when late resolutions are received. This is also the method that is followed by the House of Delegates of the American Medical Association. The House Committee on Bylaws received testimony that this method is orderly and efficient.

The House Committee on Bylaws, therefore, recommends **APPROVAL** of Resolution 85-62.

*The House Committee on Bylaws made two editorial changes to Resolution 85-62. The word "should" in the seventh line of the first Resolve and in the first line of the second Resolve has been changed to read "shall". The sentence in the first resolve will now read; "All resolutions submitted *by mem-*

bers of the House of Delegates (*pursuant to Article III, Section 3, paragraph 3*) [component county medical societies, district branches, scientific sections, and medical schools] to be presented to the House of Delegates [should] *shall* be forwarded to the speaker at least [forty-five] *thirty* days in advance of the annual meeting of the House of Delegates and referred by him to the appropriate reference committees; [and all resolutions sent in subsequent to forty-five days should be presented to the House and referred to the appropriate reference committees."]

The sentence in the second Resolve will now read; "Resolutions to be presented to the House of Delegates [should] *shall* be forwarded to the speaker at least thirty days in advance of the annual meeting of the House of Delegates.

Your chairman would like to thank, in addition to the members of the Committee and the physicians who testified before it, those members of the staff who have greatly helped this Committee; Donald R. Moy, J.D., General Counsel, and Mrs. Joan Grimm and Ms. Kathleen Curran for their secretarial assistance.

Respectfully submitted,

George Lim, M.D., *Chairman*

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The July issue of the **New York State Journal of Medicine** is the most comprehensive and disturbing ever published by a medical journal on the subject of smoking.

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The salary will be negotiated with the candidate.

Qualifed candidates are asked to submit prior to February 1, 1986 a letter and their curriculum vitae to: Alfred Gellhorn, M.D., Chairman, Search Committee for Director of Roswell Park Memorial Institute, New York State Department of Health, Corning Tower Building, Room 910, Empire State Plaza, Albany, New York 12237, (518) 474-6416.

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AIDS

A Special Bonus Program

An update on AIDS to be presented by the Medical Society of the State of New York at the 1986 Annual CME Assembly, Friday, March 7, and Saturday, March 8, from 10 AM to 1 PM.

This session has been prepared by, and will be moderated by Mark H. Kaplan, M.D., Chief of Infectious Diseases, North Shore University Hospital, Manhasset, New York.

Title and speakers will be announced in **News of New York.**

Medical Society of the State of New York

ANNUAL CME ASSEMBLY

Maintaining the Quality of
Health Care into the 21st Century.

March 7–9, 1986

and the

Annual Meeting of the House of Delegates March 6–9, 1986

The New York Hilton
New York City

COURTESY N.Y. CONVENTION & VISITORS BUREAU

HIGHLIGHTS . . .

- 22 Sessions
- Panel Discussions
- Technical Exhibits
- President's Dinner Dance

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GENERAL INFORMATION

The Medical Society of the State of New York invites you to attend its 1986 Annual CME Assembly to be held March 7–9, at the New York Hilton. The Continuing Medical Education Sessions and Technical Exhibits are open to all physicians, their guests and the allied professions. The two and a half days of meetings will provide the individual physician with a possible 18 credits out of a total of 93 Category 1, CME credit hours being offered. Over 120 outstanding speakers, including a number from out-of-state, will present papers at 22 sessions.

The theme of the CME Sessions will be "Maintaining The Quality of Health Care Into The 21st Century." A few of the subjects to be presented are, Alcoholism and Gastroenterology; Realistic Uses of Computers in Medical Practice; Evaluation and Management of Temporal Mandibular Joint Disorders; Laser Therapy in Urogenital Disorders; and An Overview of Geriatric Psychiatry. For details, see the Preliminary Program which appears in the December 1985 issue of the *New York State Journal of Medicine*. Our program will offer the clinician new approaches in diagnosis and treatment of diseases in a wide range of medical specialties.

COURTESY NEW YORK CONVENTION AND VISITORS BUREAU

MUSEUM OF MODERN ART SCULPTURE GARDEN

Comments from attendees at the 1985 CME Assembly were: 'The Speakers are excellent and well-informed'; 'The presentation was timely, and the material was well illustrated'; 'My time was well spent'. Don't miss this opportunity to gain Category 1 credits over a weekend when you are free from office hours. Why not bring your family. There is no registration fee for MSSNY members. Professional representatives from more than 50 companies will be in the Rhinelander Gallery Exhibit Hall to discuss their products and services. The Technical Exhibits will include drug products, clinical laboratories, office equipment, computer services, educational, insurance protection, and financial services, career opportunities and more.

SPECIAL EVENTS

Thursday, March 6

The Annual Dinner Dance will be held in the Trianon Ballroom of the New York Hilton, in honor of Daniel F. O'Keeffe, M.D., President, preceded by a reception in the Mercury Ballroom at 7:00 p.m. All attendees are welcome. Tickets are $75.00 per person and should be ordered in advance from the Medical Society.

Friday, March 7 and Saturday, March 8

A reception for physicians, their guests, the allied professions and exhibitors will be held on both days in the Exhibit Hall between 5:00 p.m. and 6:00 p.m., compliments of the Medical Society of the State of New York. A free drawing for a color TV set will take place at both receptions.

HOTEL RESERVATIONS

Physicians must make their own reservations with the New York Hilton no later than February 13, 1986. After that date, rooms are on an availability basis only. If making reservations by telephone, please mention that you are attending the Medical Society Convention for billing at the special rate.

REGISTRATION

CME Registration will take place in the Rhinelander Gallery Exhibit Hall, located on the 2nd floor which is accessible by escalators from the lobby. Friday, March 7 and Saturday, March 8 from 8:30 a.m. to 5:00 p.m.; Sunday, March 9 from 8:30 a.m. to 12:30 p.m.

House of Delegates Registration will take place on the 2nd and 3rd floor promenades at the following hours: Wednesday, March 5, from 12 Noon to 7:30 p.m.; Thursday, March 6, Friday, March 7 and Saturday, March 8, from 8:30 a.m. to 5:30 p.m. and Sunday, March 9 from 8:30 a.m. to 12 Noon. All MSSNY members are welcome.

CME MEETING HOURS

Friday, March 7 —10 a.m.–1 p.m.
2 p.m.–5 p.m.

Saturday, March 8—10 a.m.–1 p.m.
2 p.m.–5 p.m.

Sunday, March 9 —10 a.m.–1 p.m.

EXHIBIT HOURS

Friday, March 7 —9 a.m.–11 a.m.
1 p.m.–6 p.m.

Saturday, March 8—9 a.m.–11 a.m.
1 p.m.–6 p.m.

Sunday, March 9 —9 a.m.–1 p.m.

1986 ANNUAL CME ASSEMBLY

Medical Society of the State of New York
New York Hilton, New York City

Maintaining the Quality of
Health Care into the 21st Century

FRIDAY, MARCH 7

10:00 a.m. 1:00 p.m.
Cardiovascular Diseases, *Beekman Parlor*
Gastroenterology/Alcoholism, *Sutton Parlor North*
Obstetrics/Gynecology, *Sutton Parlor Center*
Neurosurgery, *Sutton Parlor South*
Physical Medicine & Rehabilitation, *Regent Parlor*
Update on AIDS, *Morgan Suite*

2:00 p.m. - 5:00 p.m.
Neurology, *Beekman Parlor*
Pediatrics/Alcoholism, *Sutton Parlor North*
Chest Diseases, *Sutton Parlor Center*
Occupational & Environmental Health/Workers Comp., *Sutton Parlor South*
Medical Liability Mutual Insurance Co., *Regent Parlor*
Realistic Uses of Computers in Medical Practice, I, *Madison Suite*

SATURDAY, MARCH 8

10:00 a.m. 1:00 p.m.
Ophthalmology (All Day), *Beekman Parlor*
Internal Medicine (All Day), *Sutton Parlor North*
Hand Surgery/Anesthesiolgy (All Day), *Sutton Parlor South*
Urology/Dermatology, *Sutton Parlor Center*
Psychiatry (All Day), *Regent Parlor*
Realistic Uses of Computers in Medical Practice, II, *Madison Suite*
Update on AIDS, *Morgan Suite*

2:00 p.m. - 5:00 p.m.
Ophthalmology, *Beekman Parlor*
Internal Medicine, *Sutton Parlor North*
Otolaryngology, *Sutton Parlor Center*
Hand Surgery/Anesthesiology, *Sutton Parlor South*
Psychiatry, *Regent Parlor*

SUNDAY, MARCH 10

*9:00 a.m. - 1:00 p.m.
General Surgery/Colon & Rectal Surgery, *Beekman Parlor*

10:00 a.m. - 1:00 p.m.
Allergy & Immunology, *Sutton Parlor North*
Women's Medical Society of N.Y./Family Practice/Emergency Medicine, *Regent Parlor*
Pathology, *Sutton Parlor Center*

CME CREDITS: Each program will be eligible for CME Category 1 credits on an hour-for-hour basis.

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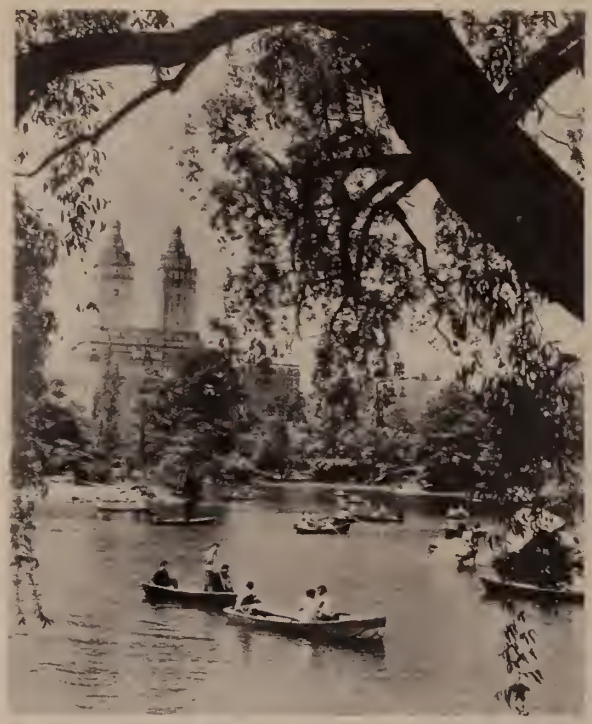

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The New York Hilton, New York City

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MISCELLANEOUS

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Feb 24–28. **Sports Medicine: 1986.** 18 Cat 1 Credits. Deer Valley Ski Resort. Info: Ms. Lisa Huber, Office of Medical Education, Children's Hospital National Medical Center, 111 Michigan Ave NW, Washington, DC 20010. Tel: (202) 745-3022.

VERMONT

Feb 4–7. **Clinical Update in Obstetrics and Gynecology.** 18 Cat 1 Credits. Stratton Mountain. Info: Maureen A. Darragh, Conference Coordinator, Office of Continuing Medical Education, Albany Medical College, 47 New Scotland Ave, Albany, NY 12208. Tel: (518) 445-5828.

VIRGINIA

Feb 3–5. **Update on Pulmonary Disorders.** Wintergreen Lodge. Info: Kathy Martin, Program Coordinator, Continuing Medical Education, Medical College of Virginia, Box 48, MCV Station, Richmond, VA 23298-0001. Tel: (804) 786-0494.

AROUND THE WORLD

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Endurance and strength exercise; the arthritic joint; re-learning control of the injured brain.

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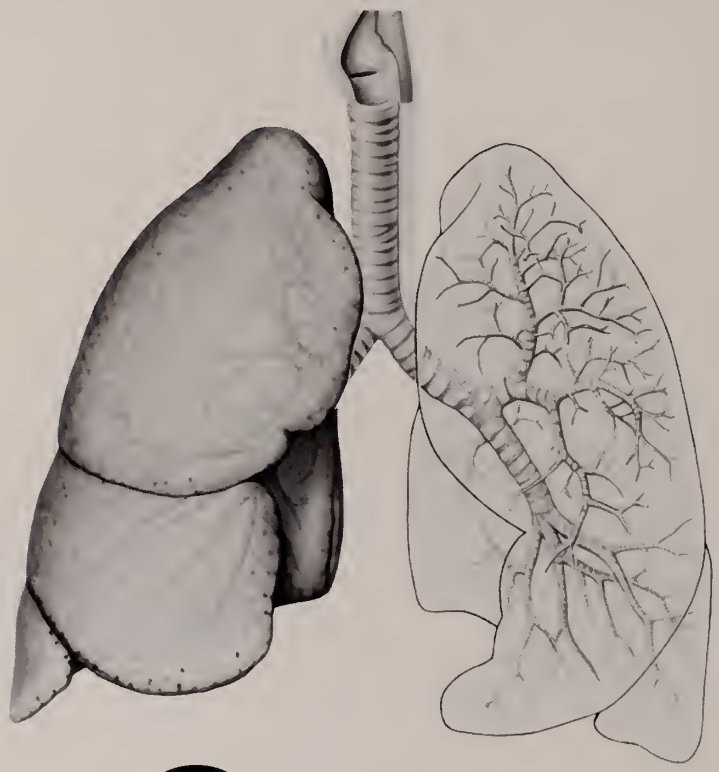

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Brief Summary Consult the package literature for prescribing information

Indications and Usage Ceclor* (cefaclor Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms

Lower respiratory infections, including pneumonia caused by *Streptococcus pneumoniae (Diplococcus pneumoniae) Haemophilus influenzae* and *S pyogenes* (group A beta-hemolytic streptococci)

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor

Contraindication Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics

Warnings IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS, INCLUDING ANAPHYLAXIS TO BOTH DRUG CLASSES

Antibiotics including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy particularly to drugs

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins and cephalosporins), therefore it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics Such colitis may range in severity from mild to life-threatening

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone In moderate to severe cases management should include sigmoidoscopy appropriate bacteriologic studies, and fluid electrolyte, and protein supplementation When the colitis does not improve after the drug has been discontinued or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile* Other causes of colitis should be ruled out

Precautions *General Precautions* — If an allergic reaction to Ceclor* (cefaclor, Lilly) occurs the drug should be discontinued, and, if necessary the patient should be treated with appropriate agents e g pressor amines, antihistamines, or corticosteroids

Prolonged use of Ceclor may result in the overgrowth of nonsusceptible organisms Careful observation of the patient is essential If superinfection occurs during therapy, appropriate measures should be taken

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs test may be due to the drug

Ceclor should be administered with caution in the presence of markedly impaired renal function Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended

As a result of administration of Ceclor, a false-positive reaction for glucose in the urine may occur This has been observed with Benedict's and Fehling's solutions and also with Clinitest* tablets but not with Tes-Tape* (Glucose Enzymatic Test Strip USP Lilly)

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis

Usage in Pregnancy — Pregnancy Category B — Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given three times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceclor* (cefaclor, Lilly) There are, however, no adequate and well-controlled studies in pregnant women Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed

Nursing Mothers — Small amounts of Ceclor have been detected in mother's milk following administration of single 500-mg doses Average levels were 0 18, 0 20, 0 21, and 0 16 mcg/ml at two, three, four, and five hours respectively Trace amounts were detected at one hour The effect on nursing infants is not known Caution should be exercised when Ceclor is administered to a nursing woman

Usage in Children — Safety and effectiveness of this product for use in infants less than one month of age have not been established

Adverse Reactions Adverse effects considered related to therapy with Ceclor are uncommon and are listed below

Gastrointestinal symptoms occur in about 2 5 percent of patients and include diarrhea (1 in 70)

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment Nausea and vomiting have been reported rarely

Hypersensitivity reactions have been reported in about 1 5 percent of patients and include morbiliform eruptions (1 in 100) Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients Cases of serum-sickness-like reactions (erythema multiforme or the above skin manifestations accompanied by arthritis/arthralgia and, frequently fever) have been reported These reactions are apparently due to hypersensitivity and have usually occurred during or following a second course of therapy with Ceclor Such reactions have been reported more frequently in children than in adults Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy No serious sequelae have been reported Antihistamines and corticosteroids appear to enhance resolution of the syndrome

Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy

Other effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients)

Causal Relationship Uncertain — Transitory abnormalities in clinical laboratory test results have been reported Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician

Hepatic — Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40)

Hematopoietic — Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40)

Renal — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200)

(0617B2R)

Note Ceclor* (cefaclor, Lilly) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections including the prophylaxis of rheumatic fever See prescribing information

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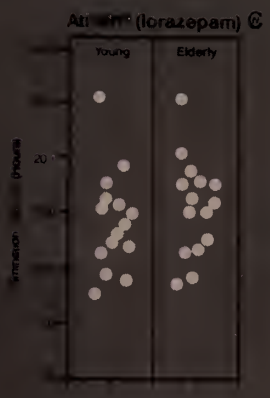
among leading benzodiazepines, has proof that its pharmacokinetics are not significantly altered by age.[1]

With Ativan, elimination half-life was very similar between young and elderly groups tested; differences did not approach statistical significance.[1]

Comparison of elimination half-lives in young and elderly subjects.



Ativan, which is *conjugated* rather than oxidized, shows little difference in half-life ($t_{1/2}$) between young and elderly subjects.[2]

References:
1. Greenblatt DJ: Clinical study, pharmacokinetics and bioavailability in the elderly, Ativan® (lorazepam). Data on file, Wyeth Laboratories.
2. Greenblatt DJ, Allen MD, Locniskar A, et al: Lorazepam kinetics in the elderly. Clin Pharmacol Ther 26:103-113, 1979.

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Brief Summary of Prescribing Information.

Indications and Usage: Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic.

Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

Contraindications: Known sensitivity to benzodiazepines or acute narrow-angle glaucoma.

Warnings: Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

Physical and Psychological Dependence: Withdrawal symptoms like those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, e.g. drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months.

Precautions: In depression accompanying anxiety, consider possibility for suicide.

For elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Terminate dosage gradually since abrupt withdrawal of any antianxiety agent may result in symptoms like those being treated: anxiety, agitation, irritability, tension, insomnia and occasional convulsions. Observe usual precautions with impaired renal or hepatic function. Where gastrointestinal or cardiovascular disorders coexist with anxiety, note that lorazepam has not been shown of significant benefit in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats, treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 6 times maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment was withdrawn within 2 months of first observation. Clinical significance is unknown; but use of lorazepam for prolonged periods and in geriatrics requires caution and frequent monitoring for symptoms of upper G.I. disease. Safety and effectiveness in children under 12 years have not been established.

ESSENTIAL LABORATORY TESTS: Some patients have developed leukopenia; some have had elevations of LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

CARCINOGENESIS AND MUTAGENESIS: No evidence of carcinogenic potential emerged in rats during an 18-month study. No studies regarding mutagenesis have been performed.

PREGNANCY: Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although all these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of discontinuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

NURSING MOTHERS: It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

Adverse Reactions, if they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%) and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbance, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and unsteadiness increased with age. Small decreases in blood pressure have been noted but are not clinically significant, probably being related to relief of anxiety.

Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

Overdosage: In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce vomiting and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol Bitartrate Injection U.S.P. Usefulness of dialysis has not been determined.

Ativan® (IV) for (lorazepam) Anxiety

DOSAGE: Individualize for maximum beneficial effects. Increase dose gradually when needed, giving higher evening dose before increasing daytime doses. Anxiety, usually 2-3mg/day given b.i.d. or t.i.d.; dosage may vary from 1 to 10mg/day in divided doses. For elderly or debilitated, initially 1-2mg/day; insomnia due to anxiety or transient situational stress, 2-4mg h.s.

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MARCH 1986

AROUND THE STATE

MANHATTAN

Mar 3–7. **Anesthesiology: Comprehensive Review V.** 48 Cat 1 Credits. Info: Registration Office, NYU Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Mar 4–7. **Seventh International Conference on Myasthenia Gravis.** Essex House. Info: Conference Director, The New York Academy of Science, 2 East 63rd St, New York, NY 10021.

Mar 13–14. **Third Annual Advances in Cancer Treatment Research.** Grand Hyatt. 15 Cat 1 Credits. Info: Office of Continuing Medical Education, Albert Einstein College of Medicine/Montefiore Medical Center, 3301 Bainbridge Ave, Bronx, NY 10467. Tel: (212) 920-6674.

Mar 13–15. **Surgical Courses in Lens Implantation.** Info: Ruth Green, Administrator, Ophthalmological Foundation of America, 823 United Nations Pl, New York, NY 10017. Tel: (212) 986-4848.

Mar 15. **The Brain and Emotion: The Neuropsychology of Affect.** New York University School of Medicine. Info: Tom Kay, PhD, Department of Behavioral Science, Institute for Rehabilitation Medicine, 400 East 34 St, New York, NY 10016.

Mar 24–26. **A Workshop on the Role of Newer Drugs in the Treatment of Common Diseases.** Info: Registration Services, American College of Physicians, 4200 Pine St, Philadelphia, PA 19104.

Mar 26. **Perspectives on Changing Reimbursement: The New Economics of**

(*Continued on p 6A*)

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Medical Care. Warwick Hotel. 6 Cat 1 Credits. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

BROOKLYN

Mar 5. **Large Granular Lymphocytes in Health and Disease.** *Mar 12.* **T-Cell Receptors: Structure and Genomic Organization.** *Mar 19.* **Treatment of Hodgkin's Disease.** *Mar 26.* **New Advances in Therapy of Advanced Bladder Cancer.** Info: Interfaith Medical Center, 555 Prospect Pl, Brooklyn, NY 11238. Tel: (718) 240-1211.

QUEENS

Mar 7. **The Bomb, the Mind, and the Future: Challenges for the Mental Health Professional.** *Mar 19.* **One-Day Course in Colo-Rectal Cancer.** 7 Cat 1 Credits. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

NASSAU

Mar 5. **Future Approaches to Type I Diabetes.** *Mar 19.* **Marrow Transplantation in Leukemia and Hemolytic Diseases.** Info: Medical Education Department, Mercy Hospital, 1000 North Village Ave, Rockville Centre, NY 11570. Tel: (516) 255-2260.

Mar 7. **Oncology and Nuclear Medicine.** Info: Medical Staff Office, Long Beach Memorial Hospital, 455 East Bay Dr, Long Beach, NY 11561. Tel: (516) 432-8000.

Mar 11. **Human Insulin.** 1 Cat 1 Credit. *Mar 25.* **Cost-Conscious Antibiotic Use.** 1 Cat 1 Credit. Info: The Community Hospital at Glen Cove, St. Andrews La, Glen Cove, NY 11542. Tel: (516) 676-5000.

Mar 15. **1986 Topics in Sports Medicine.** 7 Cat 1 Credits. Info: Louise Mandel, Director, Department of Health Education, North Shore University Hospital, 300 Community Dr, Manhasset, NY 11030. Tel: (516) 562-3045.

Mar 21. **Selected Topics in Neurology.** 6 Cat 1 Credits. Info: Bernard W. Berkowitz, MD, Department of Neurology, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-3107.

SUFFOLK

Mar 4. **Pediatric Radiology: Confidence Levels of Radiologic Examination in Children.** *Mar 11.* **Current Topics in Pediatric Dentistry.** *Mar 18.* **Cardiology: Diagnostic Advances in Non-Invasive Cardiology.** Info: Arthur J. Schwager, MD, Director, Continuing Pediatric Medical Education, Huntington Hospital, Park Ave, Huntington, NY 11743. Tel: (516) 427-0530.

Mar 22–26. **12th Annual Family Medicine Update.** 37½ Cat 1 Credits. Info: Judy V. Lum, Assistant to the Associate Dean for CME, School of Medicine (HSC), 4L, Room 170, SUNY at Stony Brook, Stony Brook, NY 11794-8437. Tel: (516) 444-2094.

WESTCHESTER

Mar 13. **Third Annual Symposium on Bone Marrow Transplantation.** 3 Cat 1 Credits. Info: Tauseef Ahmed, MD, Director of Bone Marrow Transplantation Services, New York Medical College, Westchester County Medical Center, Valhalla, NY 10595. Tel: (914) 347-4940.

MONROE

Mar 22. **Ninth Annual Spring Seminar in Anesthesiology.** 6 Cat 1 Credits. Info: Department of Anesthesiology, The Genesee Hospital, 224 Alexander St, Rochester, NY 10467. Tel: (716) 263-5265.

AROUND THE NATION

CALIFORNIA

Mar 6–8. **International Conference on Monoclonal Antibody Immunoconjugants for Cancer.** 19 Cat 1 Credits. *Mar 7–9.* **Cardiology for the Primary Care Physician.** 18 Cat 1 Credits. *Mar 10–14.* **Family Practice Refresher Course—1986.** 29 Cat 1 Credits. Info: Cynthia Saxe, Office of Continuing Medical Education, University of California San Diego School of Medicine, M-017, La Jolla, CA 92093. Tel: (619) 452-3940.

(*Continued on p 19A*)

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References:
1. Strauss WE, McIntyre KM, Parisi AF, et al: Safety and efficacy of diltiazem hydrochloride for the treatment of stable angina pectoris: Report of a cooperative clinical trial. Am J Cardiol 49:560-566, 1982.
2. Pool PE, Seagren SC, Bonanno JA, et al: The treatment of exercise-inducible chronic stable angina with diltiazem: Effect on treadmill exercise. Chest 78 (July suppl):234-238, 1980.

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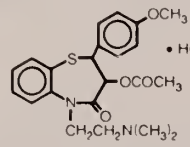
DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy)-5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+)-cis- The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina: CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect, cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given; a 120 mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women, therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** – CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

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Another patient benefit product from

PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC
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Is the longevity gender gap decreasing?

During the past few decades there has been a noticeable increase in the male-female longevity difference (MFLD) as indicated in the Monthly Vital Statistics Reports and the Annual Reports of the Vital Statistics of the USA, published by the National Center for Health Statistics.[1] According to these reports, the difference in average life span between men and women was reported as 1:2 years in the 1920s. By the 1970s excess life expectancy for women was approaching eight years and it appeared that the life expectancy difference would continue to increase. Many theories have been offered to explain this recent trend although only one appears to explain all the data, including the recent peaking and slight decline in the MFLD.

The first major publication noting the difference in the life expectancy between men and women was probably *The Natural Superiority of Women*,[2] which considered the present male-female longevity difference to be due to genetic factors. This theory was also supported by the geneticist and statistician Fisher,[3] who postulated that those with "weaker constitutions" were the ones most likely to start smoking and also to die earlier. He consistently advocated the constitutional hypothesis as the most valid reason that smokers die earlier than nonsmokers. Although this genetic theory has been replaced in prominence by other theories, a number of recent reports in journals and in the popular press have used this explanation for the male-female longevity difference.[4-6] Estelle Ramey, one of the leading present-day advocates of this theory, reports in *Prevention*: "Women are genetically stronger . . . and it's because of the double X chromosome."[4] In a recent article in *Parade* magazine, she makes a similar statement: "The feminine advantage is due partly to simple biology. Women have two X chromosomes rather than an X and Y, so they are protected from diseases caused by defective genes on one X chromosome."[5] In *The Actuarial Update* Ramey further states: "Throughout the mammalian kingdom, the male is more fragile than the female. Men are delicate!"[6]

Despite conflicting research results, the next theory to gain acceptance, particularly with obstetricians and gynecologists, has been referred to as the female hormone protection theory.[7] This theory is based on the observation that prior to menopause women have a lower incidence of cardiovascular disease (CVD) than men. After menopause, however, their CVD mortality rate appears to approach that of men, although the male mortality rate still remains higher.[8] Thus the theory was developed that female hormones—that are present in higher concentrations in women during the menstrual cycles—are the probable cause of this noticeable difference in CVD mortality. This theory was noted in the medical literature [9,10] and also at obstetrical and cardiology conferences.

During the 1960s the theory that increased longevity differences between men and women may be caused by differences in stress was published by Rosenman and Friedman.[11] This theory postulates that men who have stress-related jobs have a higher incidence of cardiovascular disease (ie, develop coronary-prone behavior) than women who are normally not subjected to such stress. Many reports by the Western Collaborative Group have dealt with Type A and Type B behavior.[12,13] The Type A (coronary-prone behavior pattern) person is one who cannot adjust to stress on the job, while the Type B (noncoronary-prone behavior pattern) is able to do so, thus accounting for his or her lower CVD rate.

A recent theory attempting to explain the difference in male-female longevity proposes that it is due to smoking. The initial works by Preston[14] and Retherford[15] have shown the strong influence of smoking on the MFLD. The study by Preston was of mortality patterns on an international level. He concluded that smoking was a major contributing factor to the MFLD in developing nations. The study by Retherford provided estimates that cigarette

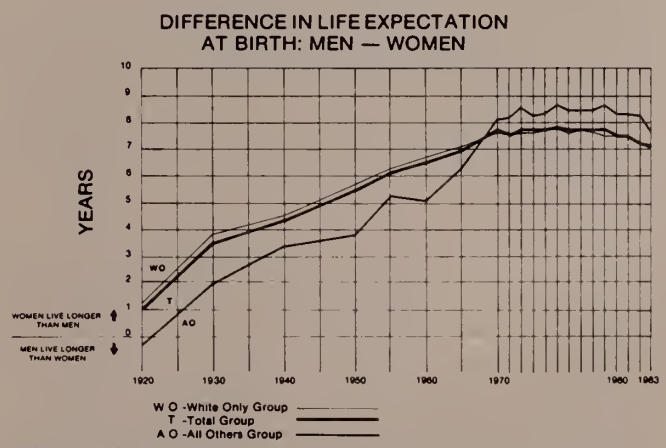

FIGURE. Graph showing more than six decades (1920 to 1983) of recording the MFLD for three distinct groups: Total, Whites Only, and All Others (comprised predominately of blacks).

smoking was responsible for between 47% and 75% of the MFLD. A recent study by Miller and Gerstein[16] provided data comparing nonsmoking men with nonsmoking women. Life expectancy appears to be similar in both instances.

Examination of the data in the Figure reveals that from 1920 to 1930 there was a greater than two-year increase in the MFLD for all groups. The men in the All Others group lived slightly longer than women in 1920; however, in the following 60 years women were living nearly nine years longer than men. From 1930 through 1960 there was an average increase of one year for the MFLD per decade in all groups. From 1960 to 1970 the group consisting of Whites Only and the Total group had a one-year gain in MFLD, while a three-year gain was noted for the All Others group. For the decade from 1970 to 1980, there appears to be a peaking of the MFLD at 7.8 years for the Whites Only and Total groups and a peaking at 8.8 years for the All Others group, and from 1980 and onward the MFLD appears to narrow for both the Whites Only and Total groups. The MFLD also appears to have declined by nearly one year during that time.

Further analysis of the Figure shows that the predicted increase in longevity difference between men and women of over eight years has not materialized except for the All Others group, which is composed predominately of black persons. In fact, for the Whites Only group there appears to be a reduction of slightly less than one year in the MFLD. The final 1983 calculation of the MFLD (7.0 years) is slightly less than it was at the time of the 1964 Surgeon General's Report,[17] that was the first major report showing the life-shortening impact of smoking. Consideration of the data in the Figure suggests that the MFLD may have peaked and is perhaps beginning to narrow.

While some arguments may be used to explain these trends by using the male genetic inferiority theory, the female hormone protection theory, or the stress theory, it would appear that the smoking theory may provide the best explanation. According to the genetic and hormone protection theories, these differences should change very little with time, thus making them less likely explanations for the changes in life expectancy observed for the past few decades, and particularly the past few years.

A consideration of cigarette smoking patterns reveals that prior to World War I only a small percentage of men smoked for long periods of time. However, during World War I cigarettes were heavily advertised and associated with support of the war. They were made easily available to the military, and smoking eventually became popular, especially for those persons with high incomes and for servicemen.

Until World War II, most black persons had little extra money to buy cigarettes. They were issued cigarettes in the service and those individuals with high-paying defense jobs could afford to buy cigarettes. Thus blacks were introduced to cigarettes several decades later than the Whites Only group. This delay in taking up smoking may explain why the MFLD for the All Others group was a year or two less than the Whites Only group from 1920 to 1960.

By 1980 the total smoking years of the black population had approached that of the Whites Only group. Many white men stopped smoking after the 1964 Surgeon General's Report, while proportionately fewer blacks reported that they had quit.[18] This large increase in MFLD for the All Others group appears to reflect the great increase in smoking by blacks that may lead to increased early mortality. Thus the All Others group that had started out with a male advantage in 1920, showed a higher MFLD than the Whites Only group in the 1970s and 1980s when their total smoking years became similar to the Whites Only population. A prediction in the narrowing of the gap was made by the author in a previous publication.[19]

Conversely, the smoking theory may explain the decrease in MFLD in the Whites Only population since the total smoking years of women is now approaching that of men. However, the total smoking years of women still remains far behind.

These interpretations of the MFLD trends are only tentative. However, if the male-female longevity difference continues to decrease for the next few decades, then the cigarette smoking hypothesis will have strong support as the most likely explanation for the male-female longevity difference. Based on present trends in cigarette consumption, the total smoking years of women will gradually approach that of men in the next 40 to 50 years. If the smoking theory is correct, the MFLD will gradually disappear.

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Screening for colorectal cancer

Colorectal cancer has attracted much attention from the medical community in recent years. One important reason for this is that colorectal cancer has become one of the most common cancers in the United States. There are about 120,000 new cases occurring each year and about 60,000 deaths attributed yearly to the disease. Another reason for colorectal cancer attracting attention recently is that it is uniquely amenable to cure if diagnosed early enough in its course, or preferably even before transition from benign polyp to malignant neoplasm.

Accordingly, there has been considerable focus on early detection of colorectal cancer. Two different approaches have been recommended: fecal occult blood testing and sigmoidoscopy. In this issue of the *Journal*, Cummings and associates describe the results of a public screening program in the western part of the state utilizing stool guaiac cards.[1] One negative aspect of the study is that only 19.5% of slide recipients returned their cards. A positive side, however, is that about 7% of persons with positive hemoccult reactions were found to have colorectal carcinoma and two thirds of those individuals had either Dukes A or Dukes B lesions. This is a much higher percentage of potentially curable lesions than reported in symptomatic patients and supports the hypothesis that screening programs may improve prognosis in colorectal cancer.

Three questions related to this report deserve consideration. How may the hemoccult card submission rate be improved? How sensitive and specific is the yield from hemoccult testing? How should patients with a positive test be evaluated? A corollary issue is the role of sigmoidoscopy in the detection of colorectal cancer.

In this study, cards were distributed free of charge at pharmacies after a publicity campaign including television exposure. Two modifications of this approach have been more effective. If people are required to pay for the hemoccult cards, they are more likely to return them. Also if the cards are handed to patients by their physician or at a medical facility, the yield also increases. An attempt to reach high-risk groups, especially those with a family history of colorectal cancer or polyps, would probably be most cost efficient in terms of patient motivation and positive yield.

The rate of positivity in subjects tested, 2.3%, is within the range of 2 to 6% found in most studies.[2] Carcinoma was found in about 7% of the individuals with positive tests, a result that is actually higher than the usual yield of 2 to 5%. While specificity and sensitivity of hemoccult cards are fairly high according to this and other studies, a different impression exists in studies of hemoccult testing in patients with known carcinoma.[3] Stool testing is positive in up to 66% of cases and negative in the rest. In general, occult blood is more likely to be found in right-sided lesions. In one study 25% of carcinomas seen on sigmoidoscopy were negative for occult blood. One reason for this is that all carcinomas do not bleed and those that do may bleed intermittently. Another reason is that hemoccult testing will not respond to hemoglobin that has been degraded to porphyrins, losing peroxidase-like activity. A new test, Hemoquant, is much more accurate quantitatively as a measure of all hemoglobin in the stool.[4] It may replace hemoccult if and when it becomes more practical.

Because of the significant miss rate with current occult blood testing, especially for left-sided lesions, the use of sigmoidoscopy as an adjunct testing method is important. Current recommendations are for persons over the age of 50 to have a sigmoidoscopic examination every three to five years. Rigid sigmoidoscopy is no longer adequate as a screening test. The average passage of a rigid scope is no further than 16 cm; the discomfort of the procedure is also a deterrent to repeated examinations. Flexible sigmoidoscopy with fiberoptic instruments is much more comfortable and, more importantly, detects colorectal neoplasms more often. Fiberoptic sigmoidoscopes are available in two lengths: 30 cm and 60 cm. The longer instrument is more suitable for use by trained gastroenterologists. The shorter one has been found to be effective, and a number of programs have been established for training primary care physicians and physician's assistants in the use of the 30-cm scope.

If a patient has an unexpected carcinoma, the benefit of this testing method is obvious. More often, the neoplasm will be a benign polyp. This is important for several reasons. Polyps are unlikely to be detected via hemoccult testing unless they are 2 cm or greater in diameter. Polyps in the rectosigmoid area should lead to a follow up colonoscopy that may uncover further metachronous lesions. It is now accepted that most carcinomas arise from benign polyps. Therefore, detection of polyps via sigmoidoscopy is an important part of a detection program to improve colon cancer statistics.

Among the participating subjects who had a positive stool test, 54% had a barium enema or colonoscopy and 18% had only sigmoidoscopy performed. The remainder

of the individuals with positive test results had no invasive procedure. Unless there is an obvious explanation for a positive test such as bleeding hemorrhoids (confirmed by sigmoidoscopy) or inflammatory bowel disease, current recommendations call for sigmoidoscopy and air contrast barium enema or for total colonoscopy in all such patients.[5]

The results of the screening program reported in this issue are gratifying in that 13 individuals were offered the possibility of a curative resection of colon cancer. If physicians applied this lesson to their patients by creating a regular screening program of their own, a significant improvement may be seen in survival from colorectal carcinoma on a much broader scale.

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Hemoccult screening for colorectal cancer: Risks and benefits

In this issue of the *Journal* Cummings and associates discuss the results of a public screening program for colorectal cancer in western New York.[1] The conclusion seems obvious: mass screening with guaiac slide testing is effective and cost efficient in detecting early stage disease and consequently prolongs survival. However, many caveats and assumptions are required before this seemingly straightforward conclusion may be accepted. One assumption is that early detection affects survival. One theory regarding cancer is that it originates from a single cell growing and spreading progressively to adjacent tissues, lymph nodes, and distant organs. If this is true, early detection—assuming effective treatment—should improve survival. Evaluation of the impact of any screening program is best done by a randomized trial.[2] Randomized trials have verified the benefit of cancer screening for only two sites: the breast and the colon-rectum. However, a single randomized trial is seldom adequate to resolve all of the questions or doubts that may arise about the effectiveness of a screening procedure. For breast cancer there are several randomized trials underway in different countries to evaluate various aspects of screening.[3–5] This is in addition to a large trial of 62,000 women that was conducted in New York City in the mid 1960s.[6]

For screening of colorectal cancer, a single randomized trial was done in the mid 1960s by the Northern California Kaiser-Permanente Medical Care Program.[7] At follow-up at seven years, two deaths from colorectal cancer occurred in the screened group as opposed to ten in the unscreened group. Adjusting for varying periods of follow up in each group, there was a 4.5:1 mortality ratio for colorectal cancer in the unscreened versus screened groups. However, there are limitations in this study. It was small for this type of evaluation, with only 5,000 to 6,000 subjects in each group, and screening was performed in the context of a multiphasic checkup program in a prepaid group practice. While it may be possible to infer some benefit for screening and early detection of colorectal cancer, it is not possible to apply these results to mass screening for fecal occult blood.

In a trial of screening for occult blood from the United Kingdom, 20,500 patients from general practitioners' lists were randomly allocated to test and control groups.[8] There was a 3.6 times greater detection rate of cancer and adenoma in the test group than in the control group. In the year following the test, only one case of cancer was detected in the group that accepted the test as compared to ten cases among the control group. The pathologic stage of tumors detected in the screened group was more favorable than those of nonresponders or controls. The authors, however, recommend a larger study to determine whether long-term mortality rates are altered.

There are two large trials currently in progress in the United States, one at the Sloan-Kettering Institute for Cancer Research in which patients were randomized by calendar period, and the other in Minnesota in which 48,000 volunteers from 50 to 80 years of age were randomly allocated to one of three groups.[9–10] In each group the subjects receive a general physical examination annually that includes a digital rectal examination. In addition, one group undergoes hemoccult testing every year while another gets it every second year. The early results from

these trials are encouraging and as more data become available, these studies should provide insight into the effectiveness of screening for fecal-occult blood. However, they are unlikely to resolve the controversy.

In summary, although the evidence from randomized trials of mass hemoccult screening for colorectal cancer is favorable, it is inconclusive and it seems unlikely that this will change in the near future. Frank argues in a series of articles that the hidden costs of the test (ie, the cost of verifying false positives and false reassurance from false negative results), coupled with low-positive predictive value and questionable sensitivity preclude its use in mass screening.[11-13]

By using a mathematical model Eddy estimates that among individuals older than 40 years of age, an annual fecal-occult blood test would decrease the probability of death due to colon cancer by 20%.[14]

Although not a randomized trial, the study by Cummings and colleagues indicates the feasibility of mass screening for colorectal cancer. It shows that large numbers of people will return their slides and that this effort may be undertaken at a reasonable cost. Whether the effort actually saved lives cannot be ascertained from the data, but the findings are, at least, consistent with that hypothesis. More importantly, the study indicates that the sensitivity of fecal-occult testing is higher than previously reported. The false negative rate has been reported to be as high as 30% in patients known to have colorectal cancer.[15] However, little information on false negative rates in the general population has been available. Only two of 11,497 people screened were detected as having false negative results after 11 months of follow up in a population-based tumor registry, yielding an annual false negative rate of 0.19 per 1,000. This approach is the most rigorous way to evaluate the sensitivity of a screening test. The result is similar to that found in the British trial of patients from general practitioners' lists where the comparable estimate was 0.28 per 1,000.[8] Thus two population-based studies have found that occult screening has a much higher sensitivity than prior estimates. This should reduce concern that large numbers of patients who have negative test results might delay seeking care due to a false sense of reassurance. In this context, the present study contributes important data to the debate on the risks and benefits of hemoccult screening.

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Impact of perinatal asphyxia, mode of delivery, and duration of premature rupture of membranes on the incidence of the respiratory distress syndrome

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ABSTRACT. The impact of a latent period, perinatal asphyxia, and mode of delivery on the incidence of the respiratory distress syndrome (RDS) was retrospectively assessed in 151 preterm births.

Latent periods over a 24-hour period did not alter the incidence of RDS in any of the gestational age groups considered. RDS was more common among infants between 29 to 34 weeks with perinatal asphyxia as reflected by a low five-minute Apgar score. The mode of delivery (vaginal delivery versus cesarean section) did not influence the overall incidence of RDS. The duration of rupture of the membranes for longer than 24 hours was associated with a higher rate of chorioamnionitis and fetal sepsis but not with a higher rate of cesarean section, maternal fever, or perinatal mortality. The results suggest that perinatal asphyxia correlates best with the incidence of RDS. Since a cause/effect relationship may exist, careful antepartum and intrapartum evaluation of fetal well-being to avoid perinatal asphyxia may be the best approach for minimizing the risk of RDS in these infants.

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Premature rupture of the membranes (PROM) is a serious management problem particularly in the preterm pregnancy. In premature gestations PROM occurs in approximately 1% of all pregnancies[1,2] and is an important cause of premature labor. The challenge has always been to balance the risks of infection to the mother and infant with that of prematurity and the need for cesarean section. This is further complicated by the contradictory evidence as to whether prolonged rupture of membranes (ROM) accelerates lung maturity. In their review of the literature since 1970 Gibbs and Blanco[3] found several studies suggesting that prolonged PROM decreases the incidence of the respiratory distress syndrome (RDS),[4,5] while other researchers noted no significant effect.[6,7] The following are also factors that could potentially affect lung maturity: diabetes,[8] hypertension,[8] sex of the infant, mode of delivery,[9] and asphyxia.[10,11] The effect of each of these factors and their relative importance is also controversial, possibly as a result of differences in the patient populations studied.

This study evaluated the relative impact of some of these factors on the incidence of RDS, while controlling for others, in a large service population.

PATIENTS AND METHODS

The records of all infants born at Bronx Municipal Hospital Center of 36 weeks gestation or less, between January 1, 1980 and December 31, 1981 and the records of their mothers were reviewed retrospectively. Multiple gestations and infants of diabetic mothers were excluded as were infants with major congenital anomalies and those whose duration of ROM was unknown. Patients with chronic hypertension or pre-eclampsia, however, were included in the review.

Gestational age was assessed by correlating the best obstetrical data available with the patient's dates and the Dubowitz score of the baby. PROM was defined as rupture of the membranes prior to the onset of labor. Prolonged latency was defined as rupture of membranes for greater than 24 hours prior to delivery. RDS and its severity was defined by O_2 requirements and respirator settings as shown in Table I.

Perinatal asphyxia was defined as a five-minute Apgar score of less than 7. Neonatal sepsis was defined as the presence of positive neonatal cultures. The maternal fever index was calculated by multiplying the maximum temperature on a given day by the number of days the patient had had that temperature.

At this institution a conservative approach has been employed when PROM is encountered. The diagnosis is confirmed by spec-

TABLE I. Definition of RDS

None	No O_2 or CPAP requirements after delivery
Mild RDS	Respirator <4 h, headbox O_2 on ≤60%, or nasal CPAP ≤5; all for ≤72 h
Moderate RDS	Peak nasal CPAP >5 or Peak O_2 >60% for >72 h, respirator ≤120 h
Severe RDS	Peak pressure >30 cm H_2O for >4 h, respirator >120 h, or death

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TABLE II. Impact of the Latent Period on the Incidence and Severity of RDS

Weeks gestation	≤28		29 to 30		31 to 32		33 to 34		35 to 36	
Latency period (h)	≤24	>24	≤24	>24	≤24	>24	≤24	>24	≤24	>24
	n = 15	n = 6	n = 10	n = 7	n = 29	n = 14	n = 29	n = 18	n = 19	n = 4
None or mild RDS	3 (20%)	0 (0%)	4 (40%)	2 (29%)	14 (48%)	11 (79%)	27 (93%)	13 (72%)	18 (95%)	4 (100%)
Moderate or severe RDS	12 (80%)	6 (100%)	6 (60%)	5 (71%)	15 (52%)	3 (21%)	2 (7%)	5 (28%)	1 (5%)	0 (0%)
P value*	NS†		NS		NS		NS		NS	

* Using Fisher's Exact test.
† NS = not significant.

TABLE III. Impact of the Apgar Score on the Incidence and Severity of RDS

Weeks gestation	≤28		29 to 30		31 to 32		33 to 34		35 to 36	
Five-minute Apgar	≤6	≥7	≤6	≥7	≤6	≥7	≤6	≥7	≤6	≥7
score	n = 12	n = 9	n = 8	n = 9	n = 11	n = 32	n = 6	n = 41	n = 4	n = 19
None or mild RDS	0 (0%)	3 (33%)	0 (0%)	6 (67%)	3 (27%)	22 (69%)	2 (33%)	38 (93%)	3 (75%)	19 (100%)
Moderate or severe RDS	12 (100%)	6 (67%)	8 (100%)	3 (33%)	8 (73%)	10 (31%)	4 (67%)	3 (7%)	1 (25%)	0 (0%)
P value*	*P* = 0.06		*P* = 0.01		*P* = 0.03		*P* = 0.003		NS†	

* Using Fisher's Exact test.
† NS = not significant.

ulum and bimanual examination following which the patient is admitted to the antepartum ward until spontaneous onset of labor or signs of infection indicate the need for delivery. Tocolysis and steroids are not used.

Statistical significance was determined by using chi square with Yate's correction or Fisher's Exact test where indicated.

Results

A total of 151 women were included in the present review; 102 (67%) had a latent period of less than 24 hours and 49 (33%) had a latent period of more than 24 hours. The incidence of hypertension and pre-eclampsia was similar in the two groups; 10% and 8%, respectively.

The patients were divided into five groups according to gestational age. When comparing patients with latency periods ≤24 hours to those with latency periods >24 hours within each gestational age group (Table II), no statistically significant trend could be found in the percentage of babies with moderate to severe RDS. However, when patients with high five-minute Apgar scores (≥7) were compared to those with low five-minute Apgar scores (≤6), the incidence of moderate to severe RDS was higher among infants with perinatal asphyxia. The difference was statistically significant within the gestational groups between 29 and 34 weeks and fell short of statistical significance for the group less than 28 weeks gestation (P=0.06) using Fisher's Exact test (Table III).

The impact of the delivery method on incidence of RDS was assessed by comparing vaginal deliveries to cesarean sections; no significant difference was found between the two groups. Furthermore, no significant difference was found in the distribution of prolonged ROM between the vaginal delivery and cesarean section groups. An increase in the incidence of low Apgar scores was noted in the cesarean section group (Table IV).

Within each delivery group a prolonged latency period was not associated with a significant change in the incidence of moderate to severe RDS (Table V); however, a low Apgar score was associated with a significant increase in its incidence (Table VI).

Perinatal outcome was studied in patients with prolonged ROM as compared with those that delivered within the first 24 hours of rupture. There was significantly more amnionitis and fetal sepsis in the former group, but the cesarean section rate, maternal fever index, perinatal mortality, and percentage of infants with low Apgar scores were not significantly different (Table VII).

Finally when dividing the patients into those with and without amnionitis, there was no increase in the percentage of infants with poor Apgar scores, moderate and severe RDS, or perinatal mortality. The only significant increase was in the incidence of fetal sepsis in the amnionitis group (Table VIII).

TABLE IV. Mode of Delivery With Respect to Perinatal Outcome

	Vaginal delivery	Cesarean section	*P* value
Moderate to severe RDS	34/102 (33%)	21/49 (43%)	NS*
Low Apgar score	22/102 (22%)	19/49 (39%)	<0.02
ROM >24 hours	36/102 (35%)	13/49 (26%)	NS

* NS = not significant.

Discussion

Few obstetrical topics are represented in the literature to the same extent as PROM. Nevertheless many questions related to this subject remain unsettled. As a result the management of premature gestations with ROM has ranged from active intervention with induction of labor within a certain interval of PROM, to more conservative approaches. Earlier reports underlying the danger of infection following prolonged ROM advocated induction of labor as a means of lowering the increased perinatal mortality noted after 24 hours of ROM.[12,13] Later reports pointing towards prematurity as a major cause of perinatal mortality and morbidity suggested that a conservative approach would be more logical. The rationale was further enhanced by reports of accelerated lung maturation with increased duration of PROM.[8] Since RDS and its sequelae continue to be a leading cause of perinatal morbidity and mortality in these age groups, this finding is of practical importance. The gestational age at which a posi-

TABLE V. Impact of Latency Period on the Incidence and Severity of RDS by Delivery Type

	Vaginal delivery		Cesarean section	
Duration of PROM	≤24	>24	≤24	>24
	n = 66	n = 36	n = 36	n = 13
None or mild RDS	46 (70%)	22 (61%)	20 (56%)	8 (62%)
Moderate or severe RDS	20 (30%)	14 (39%)	16 (44%)	5 (38%)
P value	NS*		NS	

* NS = not significant.

TABLE VI. Impact of Apgar Score on the Incidence and Severity of RDS by Delivery Type

	Vaginal delivery		Cesarean section	
Five-minute Apgar score	≤6 n = 22	≥7 n = 80	≤6 n = 19	≥7 n = 30
None or mild RDS	3 (14%)	65 (81%)	5 (26%)	23 (77%)
Moderate or severe RDS	19 (86%)	15 (19%)	14 (74%)	7 (23%)
P value	$P < 0.001$		$P < 0.001$	

tive correlation between prolonged ROM and a reduction in RDS could be demonstrated varied; some authors reported a positive relationship for all gestational age groups less than 36 weeks[14] while others only for patients more than 31 weeks.[15] One series failed to find any correlation whatsoever.[6] Many studies are handicapped by including too many variables in their analyses. This was overcome in the study reported here by eliminating multiple gestations and diabetics, and by analyzing the other variables in detail. The incidence of hypertension was equal in each group, and steroids were not used.

In analyzing the data the patients were separated into two-week gestational age groups. Larger divisions tend to be misleading since fetuses are studied whose outcome would be markedly different based on gestational age alone. No difference was found in the incidence of RDS between infants with less than 24 hours of ROM and those with more than 24 hours of ROM in any of the gestational age groups.

Another important factor that has been correlated with the incidence of RDS but has not received as much attention is perinatal asphyxia. Hobel and associates[10] reported a higher incidence of RDS among premature infants with abnormal heart rate patterns. These findings were confirmed several years later by Martin and colleagues.[11] Worthington and coworkers[16] were unable to find a significant difference in RDS between infants with and without asphyxia.

In the series reported on here perinatal asphyxia—defined as a five-minute Apgar score less than 7—correlated well with RDS. The incidence of RDS among these infants was significantly greater than in the nonasphyxiated infants in the gestational intervals between 29 and 34 weeks. The association between the two groups has been explained by the inhibition of the biochemical pathways leading to the production of surfactant in the presence of acidosis. Gluck and colleagues[17] have initially identified phosphatidyl ethanolamine (PE) methylation as the pathway inhibited by hypoxia and acidosis. However, a more recent report[18] suggests that the major pathway choline-incorporation seems to be affected as well. It is not surprising that the 29 to 34 week interval should be the group most seriously affected since it is during this period that the greatest surge in surfactant production occurs.

The impact of the mode of delivery on the incidence of RDS is unclear. Several reports suggests that cesarean section delivery places the infant at risk for developing RDS.[9] In the series reported here no difference could be demonstrated between vaginal deliveries and those infants delivered by cesarean section. Both methods were comparable in terms of duration of ROM. The increase in low five-minute Apgar scores in the cesarean section group is probably related to the fact that 16 of the cesarean sections were done because of fetal distress.

The overall incidence of perinatal asphyxia as reflected by low five-minute Apgar scores was 37%, a rate comparable to that found in other reports.[20] This incidence is much higher than the 3 to 5% incidence expected at term, although the reason for this is not known. Reid,[19] studying placentas from mothers with prolonged ROM but no apparent signs of infection, describes extensive capillary exudates and postulates that subclinical infection might be responsible for the asphyxia noticed in some of these infants. Furthermore, pregnancies associated with oligohydramnios have a higher incidence of abnormal heart rate pattern due to cord compression. These infants seem to be at increased risk for perinatal asphyxia and careful monitoring of fetal status in the antepartum period seems warranted.

In this series the risk of chorioamnionitis was significantly higher among those patients with ROM greater than 24 hours. This is consistent with previous reports,[20] but differs with Schreiber and associates[7] who found no increase in the incidence of chorioamnionitis with varying duration of PROM. The difference might be explained by the high incidence of chorioamnionitis (30%) seen among their patients experiencing less than 24 hours of PROM, which is similar to that of the patients in this report with ROM of more than 24 hours duration. Maternal fever was not a good indicator of fetal mortality, although neonatal sepsis was significantly higher in infants born to women with chorioamnionitis. There were no cases of perinatal mortality due to sepsis in this series.

In summary the results reported here are not consistent with a decrease in the incidence of RDS in patients with prolonged ROM. Perinatal asphyxia, however, appears to

TABLE VII. Impact of Latency Period on Obstetrical and Perinatal Parameters

	Latency period (h) ≤24 n = 102	>24 n = 49	*P* value
Chorioamnionitis	10 (10%)	14 (29%)	$P < 0.01$
Fetal sepsis	7 (7%)	9 (18%)	$P < 0.05$
Cesarean section	36 (35%)	13 (27%)	NS*
Maternal fever index	2.74 ± 7.1	0.93 ± 1.92	NS
Perinatal mortality	10 (10%)	4 (8%)	NS
Five-minute Apgar score ≤6	29 (28%)	12 (24%)	NS

* NS = not significant.

TABLE VIII. Impact of Amnionitis on Obstetrical and Perinatal Parameters

	Chorio-amnionitis n = 24	No chorio-amnionitis n = 127	*P* value
Five-minute Apgar score ≤6	9 (38%)	32 (25%)	NS*
Moderate or severe RDS	11 (46%)	44 (35%)	NS
Perinatal mortality	2 (8%)	12 (9%)	NS
Fetal sepsis	8 (33%)	8 (6%)	$P < 0.001$
Cesarean section	10 (42%)	39 (31%)	NS

* NS = not significant.

be one of the most important obstetrical variables that correlates well with RDS—especially between 29 and 34 weeks—and this may well be the area where obstetrical management could make a significant impact on the incidence of RDS.[21] Therefore in cases of PROM where conservative management is contemplated, adequate antepartum monitoring of fetal condition is necessary, in addition to routine surveillance for chorioamnionitis. During labor continuous fetal monitoring with scalp sampling is necessary to anticipate and possibly avert fetal acidosis. Atraumatic delivery of a nonasphyxiated baby will not only reduce the incidence of neurologic sequelae, but may also reduce the incidence of RDS between 29 and 34 weeks of gestation and improve overall perinatal outcome.

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FROM THE LIBRARY

RUPTURE OF THE WOMB

On July 5th, I received a hasty message from my friend, Dr. I., to visit a patient on whom he was in attendance, some eight miles distant, requesting me to bring my case of obstetrical instruments with me. I repaired at once to the place with the least possible delay, and on entering the house found a woman of Irish nativity, some thirty-five or thirty-six years old, and weighing about two hundred pounds, having previously borne a number of children. She had been in labor some eight hours and death was evidently near at hand.

Dr. I. informed me that he had been called there some six or seven hours previous, and for some three or four hours the labor seemed to progress unusually well, the presentation being natural and the womb almost fully dilated, with strong expulsive efforts; in fact every thing giving promise of a speedy delivery, when suddenly a remarkable change took place at once arresting the course of the labor, and placing the patient in a situation, to him, entirely inexplicable.

She complained bitterly of an unnatural and terribly tormenting pain high up in the pelvis or "body," creating the most intense agony. The pulse soon began to flag, became irregular and quick; the abdomen became tender to the touch; the countenance anxious and dejected; respiration became laborious and painful, and finally hiccough and vomiting, with coldness of the extremities soon followed. On hearing this short and hasty narration of the events above enumerated, I gave it as my decided opinion that rupture of the uterus must have taken place, to which opinion my friend, Dr. I., took strong exceptions. No time, however, could be spared for any argument in the case, and as the head still remained engaged in the pelvis, I proposed immediate delivery by means of the forceps, it being my invariable rule never to allow a woman to die undelivered so long as I possessed the means and ability to accomplish so desirable an object.

C. V. BARNETT, MD

(*Trans Med Soc State NY* 1861; 137:163–164.)

Results of a public screening program for colorectal cancer

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ABSTRACT. A public screening program for colorectal cancer was conducted in western New York in February 1984; 58,934 stool guaiac slide kits were distributed free of charge through community drugstores. A total of 11,497 (19.5%) slides were returned for testing of which 264 were positive (2.3%). Of the individuals with positive test results 202 were seen by a physician after screening for further evaluation. Colorectal cancer was found in 17 cases through screening, and 12 of these cases had early stage disease. In addition, adenomatous polyps were found in 22 patients. Follow up of screening program participants who had negative test results revealed two cases of colorectal cancer. The results from this study provide evidence that screening for fecal occult blood by guaiac testing is effective in detecting early stage colorectal cancer. In addition, the test may also be useful in detecting adenomatous polyps, a lesion often found as a precursor of carcinoma.

(NY State J Med 1986; 86:68-72)

Colorectal cancer is the most common cancer affecting both men and women and is the second leading cause of cancer deaths among persons in the United States today.[1] Despite advances made in the treatment of cancer, the five-year survival rate for patients with cancer of the colon and rectum has changed little over the last 30 years.[2] The best known predictor of patient survival is the extent of tumor spread at the time of diagnosis.[3,4] The five-year survival rate for patients with serosal penetration and negative nodes is 77% as compared to 47% for patients with regional lymph node involvement.[5] Only about 40% of patients with colorectal cancer are detected in a localized stage of disease when available methods of treatment are most effective.[6]

On the basis of the association between stage of disease at diagnosis and survival rate, cancer control efforts have focused on early detection through screening as a means of reducing colorectal cancer mortality. Since most colorectal cancers bleed intermittently,[7] and because colon cancers are often situated beyond the reach of the rigid sigmoidoscope, many groups have advocated screening for fecal occult blood as a way of identifying persons with colorectal cancer.[8,9] However, early fecal occult blood tests were unreliable.[10] It was not until the introduction of the impregnated guaiac slide in the late 1960s, and the subsequent demonstration of its effectiveness in detecting colorectal cancer, that fecal occult blood testing became potentially applicable for mass screenings.[11,12] Despite several reports in the literature showing favorable results with the stool guaiac test,[12-16] the test has been criticized because of its lack of specificity in detecting cancer (ie, the test does not indicate the source of bleeding), and because it may fail to detect nonbleeding cancerous lesions.[8,17] Moreover the accuracy of the test depends on patient compliance with dietary restrictions and stool collection instructions.

In the following report, results from a public screening program for colorectal cancer are presented in which 58,934 stool guaiac slide kits (Hemoccult II; Smith Kline Diagnostics) were distributed through a local drugstore chain in western New York during a four week period in February 1984. Data are presented on the return rate of slides for testing, characteristics of persons screened, compliance by those persons with dietary restrictions and instructions for preparing slides, results of follow up of individuals with positive test findings, and the stage distribution and characteristics of cancer cases detected through screening.

PATIENTS AND METHODS

Stool guaiac slide kits were distributed free of charge through 18 community drugstores in Erie and Niagara counties of New York in February 1984. During the first five days of February, a local television station (WKBW—Channel 7) aired a series of educational reports on colorectal cancer during the evening news. After the first week, television promotion of the screening program was continued by periodic reports concerning the program on the news (eg, live broadcasts from drugstores where slide kits were distributed or showing technicians testing slides). Both the educational and promotional reports emphasized the importance of screening for colorectal cancer in persons older than 40 years of age.

Each slide kit included three guaiac slides; applicator sticks; a specially-designed pamphlet describing the purpose of the test, giving instructions on how to prepare slides, and dietary instructions; a plastic bag in which to insert slides before putting them in an envelope for mailing; and a prepaid, self-addressed mailing envelope. The dietary instructions advised the participants to eat plenty of fresh fruits, vegetables, and bran cereals; not to eat red meat; to avoid high peroxidase-containing foods such as turnips and horseradish; to avoid aspirin-containing medications; and to avoid taking vitamin preparations that may contain ascorbic acid

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(vitamin C) during the testing period. Individuals were instructed to continue taking any prescribed medications, and were told to collect stool specimens from three consecutive bowel movements. The test instructions requested the individuals to obtain two smears from different parts of each stool with the applicator stick and to record the date when the specimen was collected on the cover of the slide. The individuals were then instructed to return the slides in the self-addressed, prepaid envelope promptly after completion.

All of the slides were to be returned to Roswell Park Memorial Institute for testing. The slides were not rehydrated prior to testing. All persons who returned slides for testing were sent a letter within seven days informing them of their test results. Persons with negative test findings were reminded that the test is not conclusive, and that they should see a doctor if they have any other cancer symptoms. Individuals who had a positive result on any one of the three slides were told that they should see a physician as soon as possible to have their condition evaluated, but also reassured that a positive result does not necessarily indicate cancer.

Those persons with positive test results were sent a follow up questionnaire one month after being informed of their test findings in order to determine if they had been seen by a physician. Those who reported having contacted a physician were asked to indicate the name and address of the physician they had seen and to give the results of the evaluation. After four weeks nonrespondents were contacted by telephone to obtain the follow up information. To verify the information obtained from patients, physicians identified on the patient follow up questionnaires were contacted and asked if and when they had seen the patient, what diagnostic tests they had performed, and the findings of their diagnostic evaluations.

Of the 264 persons with positive screening results, 22 (8.3%) were lost to follow up because they could not be located; 31 (11.7%) refused to see a physician for further evaluation; 9 (3.4%) claimed to have been seen by a physician but refused to provide follow up information; and 202 (76.6%) saw a physician and provided information regarding their follow up visits.

The Western New York Tumor Registry was used to verify cancer cases identified through follow up and to obtain information on the date of diagnosis, location of the tumor, and extent of disease at diagnosis. (The Tumor Registry covers the following eight counties of New York State: Allegany, Cattaraugus, Chautauqua, Erie, Genesee, Niagara, Orleans, and Wyoming.) The tumor registry also was used to identify the incidence of colorectal cancer among screening program participants who had negative test findings.

To obtain a more detailed assessment of the characteristics of the individuals screened and to evaluate how closely those persons reported following the instructions for preparing slides, a brief questionnaire was mailed to a 10% random sample of persons screened. The questionnaire, along with a prepaid, self-addressed return envelope, was sent with the letter informing the person of their screening test result. A total of 829 of 1,149 questionnaires were returned, yielding a response rate of 72%.

Results

A total of 58,934 stool guaiac slide kits were distributed during the screening program; 11,497 persons (19.5%) returned the slides for testing. Of the 11,497 persons who returned slides for testing, one or more slides were positive in 264 persons (2.3%).

Table I describes the characteristics of screening program participants based on the questionnaire sent to a 10% random sample of persons screened who returned slides. Most of the individuals reported that they had followed the instructions for doing the test. Seventy-five percent of individuals reported that they did not eat red meat during the testing period, 65% percent reported that they had increased their usual consumption of vegetables and fruit, and 49% said that they ate more bran cereal than usual while they were doing the test. Of the total number of persons screened, 7% reported that they took aspirin and 8% reported taking vitamin C tablets or a multiple vitamin during the testing period. Stool specimens from three bowel movements were collected by 88% of the screened individuals and 97% reported collecting the specimens directly from the stool using the applicator sticks rather than from tissue paper. The mean number of days elapsing from collection of the first stool specimen to testing was 4.9 days (range, 1 to 50 days). Of all the specimens obtained, 98% were tested within 14 days after collection.

Of the 264 screenees, 202 (76.5%) saw a physician after screening for further evaluation and provided information about their follow up visits. Of those persons seen by a physician after screening 75% had a digital rectal examination, 63% had a barium enema, 52% had a repeat stool guaiac test, 40% underwent sigmoidoscopy, 34% had both upper and lower gastrointestinal series performed, and 29% had colonoscopic examinations. A digital rectal examination or repeat guaiac test only was performed on 25% of the screened population. Three persons with positive test results (1.4%) who reported seeing a physician after screening did not have any diagnostic tests performed. In one of the three cases the physician attributed the positive test result to the patient's diet during the testing period. In the other two cases the physician attributed the positive tests to the presence of ulcerative colitis.

The results of diagnostic evaluations on the 202 persons with positive tests who were seen by a physician after screening are shown in Table II. Colorectal cancer was detected in 17 patients (8.4%). Polyps were found in 48 persons, including 11 of the 17 cancer cases. Information pertaining to the type, size, and location of the polyps was obtained for 40 of the 48 patients. Adenomatous polyps were found in 33 of these 40 patients (11 cancer cases and 22 noncancer cases). The approximate locations of polyps detected in these 40 patients are given in Figure 1. In the 22 noncancer patients in which adenomatous polyps were detected six patients had polyps less than 1 cm in diameter, eight had polyps between 1 and 2 cm, five had polyps larger than 2 cm, and in three cases polyp size could not be determined. In the 11 cancer cases in which adenomatous polyps

TABLE I. Characteristics of Persons Screened

Average age	56.6 yr
Percent female	60.2%
Race:	
White	97.1%
Black	2.4
Other	0.5%
Educational level:	
Less than 8th grade	7.2%
Some high school	18.7%
High school graduate	40.9%
Some college or higher	33.2%
Annual family income:	
Less than $8,000	16.6%
$8,000 to $15,999	26.8%
$16,000 to $24,999	27.4%
$25,000 and over	29.2%
Percent with a family history of colorectal cancer	12.0%
Percent with a personal history of cancer	7.5%
Recency of last stool guaiac test:	
Never	70.8%
More than 3 years ago	6.7%
2 to 3 years ago	8.6%
1 to 2 years ago	9.1%
Within the past year	4.8%
How first heard about the test:	
Television (Channel 7 news)	79.4%
Display in the drugstore	6.9%
Radio or newspaper	2.3%
Doctor	5.8%
Friends or relatives	3.6%
Other	2.0%
Percent reporting evidence of blood in their stool during the past year	13.3%

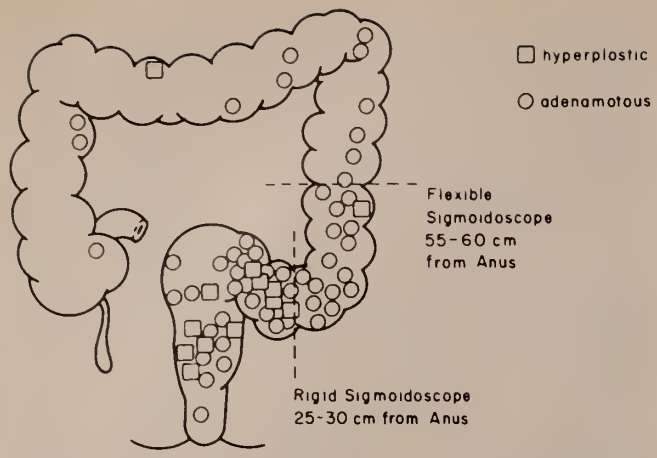

FIGURE 1. Location of polyps in 40 of 48 patients found through screening.

were found two patients had polyps less than 1 cm in diameter, two patients had polyps between 1 and 2 cm, and seven patients had polyps larger than 2 cm.

The names of all 11,497 persons participating in the screening program were checked against the names of those persons with colorectal cancer reported to the Western New York Tumor Registry between February 1, 1984 and December 31, 1984. The names of 16 of the 17 individuals identified as having cancer through screening were confirmed by the registry. The one person not identified in the registry resided and received treatment outside of western New York and therefore would not have been reported to the registry. The names of two individuals with negative test findings also appeared in the tumor registry. Both persons were found to have colorectal cancer after participating in the screening program. One of the individuals with cancer missed through screening was a 65-year-old man who was diagnosed as having leiomyosarcoma of the rectum two months after participating in the screening program. The second case missed through screening was a 76-year-old woman who was diagnosed three months after screening as having a moderately differentiated adenocarcinoma of the ascending colon.

The characteristics of the 17 cancer cases identified through screening, and the two false-negative cancer cases identified through the tumor registry search are noted in Table III. The pathologic stage of disease was determined by using the Astler-Coller modification of the Dukes classification.[18] Of the 17 cases of colorectal cancer detected through screening, 12 (70.5%) were identified in a localized stage (either in situ or modified Dukes A, B1, or B2). Figure 2 shows the location of each of the tumors found through the screening program and in the two individuals who had negative screening results but who were identified through the tumor registry search.

TABLE II. Results of Diagnostic Evaluations of Persons With Positive Test Results

Diagnosis	Physician verified report (n = 179)	Patient report only (n = 23)	Total (n = 202)
Colorectal cancer	17	—	17 (8.4%)
Hemorrhoids	64	7	71 (35.1%)
Diverticulosis	33	2	35 (17.3%)
Anal/rectal fissures	7	—	7 (3.5%)
Ulcerative colitis	5	2	7 (3.5%)
Peptic ulcer	8	2	10 (4.9%)
Adenomatous polyps	33	—	33 (16.3%)
Hyperplastic polyps	7	—	7 (3.5%)
Type of polyp not specified	—	8	8 (3.9%)
Other causes of bleeding*	10	3	13 (6.4%)
No pathology found	39	5	44 (21.8%)

Note: Percentages add to more than 100 since some patients were diagnosed with more than one condition.

* Includes the following conditions: hiatus hernia (3), gastritis (2), hemorrhagic cystitis (2), general irritation of the colon (2), melanosis coli (1), bleeding gums (1), hemorrhagic sinusitis (1), and thrombasthenia (1).

Discussion

The results obtained from this screening program and those of other programs reported in the literature[12-16] indicate that screening for fecal occult blood by using the guaiac slide test may contribute to the early detection of cancer. However, due to the potential problems of lead-time bias and length-biased sampling, it cannot be concluded from this study that screening for colorectal cancer by fecal occult blood testing can significantly reduce disease mortality.[19] The findings from this study also suggest that the test may be useful in helping to identify persons with adenomatous polyps. This may be significant since removal of these polyps may prevent the subsequent development of malignant disease.[20] However, it should be noted that from this study the researchers are unable to determine how many polyp cases were missed through screening. It is also possible that many of the incidences of polyp discovery were coincidental findings not associated with a positive guaiac test.

Television coverage proved to be an effective means for creating public interest and participation in the screening program; 79% of individuals screened reported first learning about the guaiac test from the television news reports. Of those persons who returned slides for testing, 70% had never taken the test before. The program was reasonably successful in reaching a high-risk population for colorectal cancer. Eighty-nine percent of the persons screened were over 40 years of age, and 12% reported a family history of colorectal cancer.

Approximately 20% of the slide kits distributed were returned for testing. The return rate obtained in this screening program is low in comparison to the 44% return rate obtained in a similar program conducted in Erie

TABLE III. Characteristics of Colorectal Cancer Cases

Age	Sex	No. of slides positive	Symptom history	Stage of disease
79	F	3/3	none	B2
79	M	3/3	none	B2
69	F	1/3	loose stools	C2
66	M	1/3	none	B1
74	F	2/3	rectal bleeding	in situ
55	M	3/3	none	B1
55	M	1/3	bloody stool	C1
59	F	1/3	bloody stool	B2
65	M	2/3	none	C2
77	M	3/3	none	in situ
69	M	3/3	none	in situ
67	M	2/3	none	B1
75	M	1/3	none	C2
64	M	2/3	none	B1
77	F	3/3	none	C1
71	M	1/3	rectal bleeding	B1
66	F	2/3	none	B1
65	M	0/3	rectal pain	leiomyosarcoma of the rectum
76	F	0/3	abdominal pain	B2

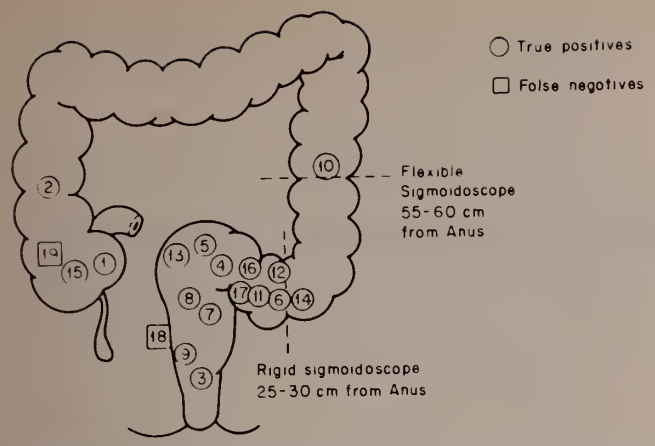

FIGURE 2. Location of cancers in the 17 cases detected through screening and in the two cases negative on screening who were identified through the tumor registry search.

County in 1982.[13] In the 1982 program, the participants were required to pay $1.00 for each slide kit. In the future, screening programs might consider charging a small fee for the slide kits to eliminate those individuals not committed to doing the test.

The rate of positive slide results was 2.3%; this is consistent with findings from other screening programs.[12-16] Three quarters of the individuals with positive test results saw a physician for additional evaluation after screening. Physician evaluations varied widely, although 72% of patients had an endoscopic examination performed—18% had sigmoidoscopy only, 25% had barium enema with or without sigmoidoscopy, and 29% had colonoscopy with or without barium enema or sigmoidoscopy. Because of variation in the diagnostic evaluations performed on persons with positive results, it is difficult to determine the error rates for the test. Of the 202 persons with positive results, 44 (39 verified by physician report) had no finding of disease that could cause blood in their stool, yielding an overall false positive rate of 3.9 per 1,000 (44 false positives out of 11,278 screened cases with no evidence of blood in the stool). However, many of the conditions discovered through screening are questionable causes of gastrointestinal bleeding (eg, hiatus hernia, diverticuloses). It is possible that in some patients the positive test finding had nothing to do with their condition. Thus the findings reported here probably underestimate the true false positive rate.

Of the 202 individuals who saw a physician after screening, 17 (8.4%) were found to have colorectal cancer. Among the 62 individuals with positive results who either were lost to follow up, refused to see a physician for further evaluation, or refused to provide information regarding their follow up physician visit, it is unlikely that any had colorectal cancer since their names did not appear in the tumor registry ten months after screening. Twelve of the 17 persons with cancer (70.5%) as detected through screening had localized disease. By comparison, in western New York between 1979 and 1981 31% of colorectal cancer cases were diagnosed in a localized stage of disease. The difference in the stage of disease distribution for screened cases and for the general population of colorectal cancer cases in western New York is statistically significant at the 5% level (chi square = 10.3, $df = 2$, $P < 0.01$).

A crude measure of the cost of case detection was made by dividing an estimate of the cost of screening by the number of persons with cancer identified through screening. Since the screening kits and television time were donated, these costs were not included in the estimate of the cost of screening. Screening costs included personnel required to test and record the screening results, follow up of individuals with positive results, postage required for mailing the screening kits to Roswell Park and letters sent to participants notifying them of their test results, and the cost of additional diagnostic evaluations for those with positive test findings. The personnel costs for testing slide kits was estimated to be $7,200. This figure was based on three full time persons working for six weeks at an hourly rate of $10. The personnel cost for follow up was estimated to be $1,200. This figure was based on one half time person working for six weeks at an hourly rate of $10. Prepaid return envelopes were given to all those who obtained slide kits in order to encourage them to send the slides back to Roswell Park for testing. However, since postage is not charged unless the envelope is used, this resulted in a cost of approximately $3,600. Letters notifying screening program participants of their test results were sent to 11,497 persons at a cost of $2,300. Follow up mailings to persons with positive results accounted for an additional $250 in postage. The estimated cost for diagnostic studies of persons with positive results was based on the cost of diagnostic tests charged at Roswell Park. These costs were then applied to the actual tests performed on those with positive test results. The estimate of the total cost of diagnostic evaluations for those with positive screening results was $50,470. Overall, the total cost of screening was estimated to be $65,020, yielding a cost per cancer case detected of $3,825. If case detection includes both patients with cancer (n = 17) and patients with adenomatous polyps (n = 22), the cost per case detected would be reduced to $1,667.

In summary, the results from this screening program suggest that public screening for fecal occult blood by using the guaiac slide test is effective in detecting colorectal cancer in an early stage of the disease. The test appears to be sensitive to the detection of colorectal cancer (89.4%), although two cases of cancer were known to have been missed through screening. The test also appears to be useful in identifying persons with adenomatous polyps. The low cost of the test relative to alternative screening procedures, its high public acceptance, and the high incidence of colorectal cancer makes this approach for detecting colorectal cancer desirable for large-scale screening efforts.

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See also pp 61–63.

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MSSNY Medical Liability Reform Fund Honor Roll

In the September 1985 issue the *Journal* began publishing the list of physicians who have generously contributed to the compaign to inform the public about the crisis in medical liability litigation. The names of additional contributors are listed below.

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Computerized dynamic simulation of clinical management

A ventilation simulation program

RAN D. ANBAR, MD, MICHAEL ANBAR, PHD

Of the many uses of computers in medicine—ranging from computerized tomography to computerized patient records and billing—the most challenging for the practicing physician are the "artificial intelligence" diagnostic programs[1-4] and the clinical case simulation programs used in medical training.[5-8] In medical education and training, computers offer the user an opportunity to diagnose and make decisions on the management of real-life penalties. Computers are also being used in medical training as comprehensive indexes of medical texts,[9] as visual aids in classroom instruction,[8,10] and as effective providers of nonillustrative and illustrative review questions in both preclinical and clinical training.[11-15] They seem to be most effective as teaching tools in presenting clinical simulations.[16-18] Analogously to computerized flight simulators, computerized clinical simulations with cue-free problem solving offer an opportunity to sharpen the clinical instincts of the user in a protected environment. It is conceivable that computer simulations will eventually become a major part of medical training.

Clinical simulations are more effective the closer they simulate clinical reality. Although a computer displays clinical data in a verbal or numeric form and without the richness and diversity of information presented in an actual physical examination, the mind can compensate for this limitation, especially when the user has had prior experience with patients. There is another limitation, however, in that most available computerized simulations lack the characteristic attributes of disease. The primary deficiency in most simulations lies in the frozen, snapshot-like nature of the presentation. Such training programs are static. They describe a fixed biologic situation and allow the user to solve the given clinical "riddle" in a sequence of steps, while the clinical information remains unchanged in the data base of the program. Thus there remains a large gap between this artificial setting and the dynamic clinical reality.

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In an actual clinical setting the patient presents a set of symptoms and signs that change continuously with the progression of the disease or as a result of interventions. In a realistic clinical simulation, the diagnostic or therapeutic actions taken by the user may change the natural course of the disease and thus significantly alter the presentation. The computer, which is designed to handle interrelated multiparameter problems, can provide ever changing clinical scenarios. Computerized dynamic simulation (CDS) that is necessary for adequate medical training may be offered even with a simple microcomputer. The computer may also present a multidescriptor picture of the patient—each symptom or sign constituting a describing parameter—that can simultaneously change with any alteration of the patient's status. This allows the user to think in a multidimensional manner and make clinical management decisions on the basis of patterns rather than single pieces of information.

There are certain clinical situations, such as intensive care or emergency medicine, where the prompt response to rapidly changing patterns of descriptors is critical. Physician training should therefore include this capability offered by CDS. A dynamic simulation continually changes the status of the simulated patient, following a path based on the current knowledge of physiology and pathophysiology. However, this status is not always predictable, and each parameter may change its value in a random fashion within reasonable limits. This so called controlled randomness along the time axis, typical of biologic behavior, is the underlying principle of CDS. The following report illustrates the operation of CDS by describing a specific program.

The usefulness of CDS has been demonstrated in a training program for physicians who manage ventilator-dependent infants in a neonatal intensive care unit. This clinical situation has been chosen to demonstrate the usefulness of CDS because it involves a complex interrelated, multiparameter situation that requires fast decisions on the basis of a rapidly changing pattern. In addition, this simulator addresses a serious need in clinical training. Management of the infant on a ventilator is one of the

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FOR AN INFANT WITH RDS:

(1) Keep pO2 60-90; A pO2 much less than 60 does not deliver enough
    oxygen to the tissues. A pO2 greater than 90 is associated with
    an increased incidence of RETROLENTAL FIBROPLASIA in the premature.

(2) Keep pH between 7.30 and 7.50 to allow for optimal enzymatic
    activity. Since it is preferable not to hyperventilate infants
    with RDS, the pH is usually run closer to 7.30.

(3) Keep PIP reasonably low since there is an increased incidence of
    trauma to the lungs with high PIPs.

(4) PEEPs should also be kept low, however they need to be high
    enough to keep airways open; these would otherwise collapse.

FOR AN INFANT WITH SUSPECTED PFC:

(1) Keep pO2 greater than 100 and pH greater than 7.40 to limit PFC.

(2) Same as (3) and (4) above.

Press 'RETURN' when ready to continue.
```

FIGURE 1A. General guidelines for the user.

```
Baby Girl Nurko was the 3.9 kg product of a 41 week gestation.
The baby is transported here today from Lawerence Memorial because of
suspected MECONIUM aspiration.

In the program which follows:

Options 1-12 offer various manipulations of the baby.

Option 13 - WAIT - allows you to observe the patient without
            manipulations for a specified number of hours.

Option 14 - REVIEW - provides a summary of all the vent settings
            and blood gases which have been utilized.

Option 15 - STOP - terminates the program and gives your score.

Option 16 - GLOSSARY - defines many of the terms in this program.

To have the above information repeated during the program
ask for 'HISTORY' to be defined in the GLOSSARY.

Would you like suggestions to be given during the program? ▮
```

FIGURE 1B. Short history and operating instructions.

major tasks facing neonatologists today. In learning how to assess the ventilatory requirements of a sick infant, medical students and house officers need to follow the progress of many babies over several weeks in order to learn the principles involved and to be able to cope with emergencies as they occur. The factors that most impede this process are the time required for ventilatory manipulations to take effect on the patient and the time necessary for the underlying disease to take its course. The computerized ventilation simulation program described here gives immediate feedback to its user regarding the effects of manipulations of the infant, and allows simulated ventilatory management for five days to take place in less than one hour—the time it takes to run a case simulation after minimal initial training. In this manner, the use of the computer allows for the rapid accumulation of clinical acumen.

Ventilatory Simulation Program

The ventilatory simulation program (VSP) was designed to provide a realistic simulation of the ventilator-dependent infant. Aside from factors that may be manipulated on the neonatal ventilator—fractional inspired oxygen (FiO_2), respiratory rate (RR), peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), and inspiratory time (IT)—the program also monitors the fluid balance of the infant, vital signs, temperature, and airway management by occasionally checking the endotracheal tube (ET) for positioning and providing for its suctioning. VSP also gives opportunities for a cursory physical examination and obtaining chest radiographs. Finally, as a further aid for teaching, VSP offers suggestions regarding the management of the ventilated infant (Fig 1) and provides a glossary for the terms used in such management.

To be a teaching tool that could be mastered in a single sitting, some necessary concessions have been made. All of the simulated infants are "paralyzed" for the purposes of the program. However, the program will eventually reverse paralysis of infants who have been managed successfully. The user is not requested to deal with hemoglobin concentration and its impact on oxygen carrying capacity. Also, intraventricular hemorrhages and their manifestations—probably the most common nonrespiratory complications of the ventilated neonate—have not been included in the current version of VSP.

VSP was written in BASIC and is run on an IBM personal computer (IBM-PC). It may be run on a monochrome or color screen and is readily transferable to other microcomputer systems. VSP uses a random generator to "create" different babies with the respiratory distress syndrome (RDS). This random "infant synthesis" takes place within certain guidelines including increasing severity and prolongation of disease for premature infants and a disease peak between two and four days of life. There is an unlimited number of "synthesized" patients, so the user will never repeat a case unless he specifically requests to do so.

Once a baby is "generated," the timing of worsening and improvement of the infant's condition may not be altered by the user's management; however, the respiratory status of the baby at any time is a direct function of the ventilatory settings chosen. An example of the report dis-

```
DAY  1    HOUR  2:30                    STATUS = ACCEPTABLE
----------------------

pH = 7.30    pO2 =  72    pCO2 =  48    HCO3 = 23    B.E. = -0.6

FiO2 = 0.40  RR = 23      PIP = 22      PEEP =  3    I-TIME = 1.5
                                                     E-TIME = 1.1

Last CXR (On DAY 1 : HOUR  2 : X-RAY # 1) showed:
Slight diffuse granularity throughout all lung fields.
OPTIONS:

(1) Change FiO2     (6) Suction/chest PT     (11) Obtain new CXR
(2) Change RR       (7) Decompress stomach   (12) Alter fluids
(3) Change PIP      (8) Check ET tube        (13) WAIT   (14) REVIEW
(4) Change PEEP     (9) Insert chest tube    **********************
(5) Change I-TIME   (10) Physical exam       (15) STOP   (16) GLOSSARY

Please enter option number followed by 'RETURN': 2▮
```

FIGURE 2. Patient's status display screen with the options for actions in the lower part. This display changes every time any action is taken (time has elapsed), except when the user looks up something in the glossary. In the glossary one can find again the history of the patient as well as an explanation of the status if it says "NEEDS INTERVENTION."

```
HEART RATE = 127

SYSTOLIC BLOOD PRESSURE = 51

TEMPERATURE (in degrees FARENHEIT) = 98.5

There is no spontaneous respiratory response.

Good breath sounds bilaterally.

Good movement of chest wall on inspiration.

There has been no urine output during the past 4 hours.
(Infants often don't urinate prior to 24 hours of age.)

Press 'RETURN' when ready to continue.
```

FIGURE 3. Typical physical examination report, obtained when choosing option 10. Similar reports and comments are displayed following most other actions.

played to the student after each intervention is presented in Figure 2; it gives the current status of the different parameters and the 16 options of action. On the IBM-PC the user has the option to receive a hard copy of any status reports by screen dumping, or a printout of any of the derived reports for further reference.

On physical examination the user can learn whether the chest wall is moving adequately with respiration and can assess the quality of the breath sounds as affected by disease state, airway status, and ventilatory pressures. The user is also provided with the patient's vital signs, that are affected in part by the patient's age (BP rises over the first 50 hours of life), weight, and volume status.[19] The WAIT option allows the user to observe the patient without manipulation for a specified amount of time. At the end of this time period another blood gas determination is made. If the user wants to wait longer than 23 hours the warning message "Do you want to wait that long on an infant in the ICU?" is displayed.

The user is provided with arterial blood gas results that reflect the respiratory pathophysiologic status of the simulated infant. The baby's response to the user's manipulations are brought about by conventional models of respiratory physiology. In VSP the arterial CO_2 tension (P_{CO_2}) is most often affected by RR, tidal volume, and expiratory time.[20] The tidal volume is estimated from the difference between PIP and PEEP, taking into account the dead space volume in the baby's respiratory tree.[19] The expiratory time (as calculated from the RR and IT) affects the P_{CO_2} only when the time provided for expiration is below 0.4 seconds. The arterial O_2 tension (P_{O_2}) is most often affected by F_{iO_2}, P_{CO_2}, and mean airway pressure. If the PEEP is too low, oxygenation is decreased.[20-23] Both the P_{CO_2} and the P_{O_2} are affected by the IT if the PIP is too high to reach within a short IT.[24] Serum bicarbonate (HCO_3) concentration is calculated by using P_{CO_2} and bicarbonate buffer curves. If the patient's fluid or circulatory status is compromised, then the resultant acidosis is reflected by a drop in serum bicarbonate. The pH is calculated by using the Henderson-Hasselbach equation, from the HCO_3 concentration and the dissolved CO_2 concentration, which is derived from the P_{CO_2}.[25]

Both the P_{CO_2} and P_{O_2} are affected adversely if suctioning is not sufficient, the stomach not decompressed, or the ET tube plugged or out of position. VSP allows the user to check the airway or stomach at any time and randomly increases airway obstruction over time if these factors are not monitored. Unlike pulmonary physiology computerized models, including those dealing with pathophysiology,[26] VSP includes purely clinical parameters and interventions such as the positioning of the ET tube, stomach decompression, or "pulmonary toilet." Moreover, the physiologic models used have a built in random noise, bringing them closer to reality.

A Typical VSP Session

After having chosen to work with the program at a certain level of sophistication (with or without comments on the actions of clinical management or warnings about impending problems) the user is presented with the following situation: a 1.1 kg baby girl has been transferred from a community hospital where she was born one hour earlier after 29 weeks of gestation. The baby was transported on a ventilator after being treated with pancuronium bromide. The emergency crew did not set the respirator properly. On arrival to the hospital the blood gas values are F_{iO_2}, 0.30; RR, 25; PIP, 13; PEEP, 3; P_{O_2}, 35 mm Hg; and P_{CO_2}, 65 mm Hg. The user rapidly adjusts the partial pressure of oxygen and the PIP to bring the blood gases within an acceptable range. After a slight adjustment of the PEEP and a physical examination that shows good chest movement and bilaterally equal chest sounds, the baby is left without intervention for four hours.

At that time there is a definite worsening of the respiratory status requiring increased F_{iO_2} and RR. The situation worsens in spite of these adjustments and there is minimal response of the blood gases even with increased PIP. The user now realizes that the ET tube position had not been checked and is now completely misaligned. An adjustment of the ET tube and decompression of the stomach changes the blood gas pattern dramatically and makes it necessary to readjust the RR and the F_{iO_2}. Leaving an unnecessarily excessive PIP results in pneumothorax five hours later. The situation is detected by physical examination and is confirmed by radiography. At this point the program comments that in an acute situation, once pneumothorax is detected on physical examination, a chest radiogram is unnecessary prior to intervention. A chest tube is then inserted to control the emergency. On physical examination the user now realizes that urine output is extremely low and orders a bolus of saline and an increase by 20 cc/kg/d of the maintenance fluid rate; neglecting the fluid balance would be reflected in changes of base excess, heart rate, and ultimately in respiratory status.

This student managed to maintain the infant's health and by the morning of the fourth day improvement in the RDS was apparent. By the end of day 5 the baby was no longer considered critical. At that time simulation is terminated and the student gets a report on this patient's management that points out the errors and omissions. At the same time he gets a printout of the blood gas history over the 120 hours of management that allows for a review of the case. Now the user may repeat the simulation with a

similar infant or one generated completely at random.

As stated earlier, there is an almost endless number of clinical situations that present themselves to the student. The case described here is representative of but not identical to other training sessions. In the following section the machinery that activates VSP is described.

Algorithms and Operational Parameters of VSP

Since the computer-generated infant continues to develop a disease throughout the simulation, it's behavior at any particular time is determined by a combination of the course of the disease and the effects of intervention. Twelve arrays of parameters that describe the basic course of the infant's disease should be studied (descriptions of a few of these arrays follow). These arrays change during the program depending on the user's and the intrinsic program's manipulations of various factors. In the description of some of these arrays, the different feedback displayed messages (DMs) the user receives in response to actions or queries are included.

Oxygen array. A linear model increases the oxygen requirement as a disease worsens (up to the peak) and then rapidly decreases the oxygen requirement. The slope of the increase is influenced by the user's manipulations. If the patient has pneumothorax the oxygen requirement increases with each successive one quarter day. If the patient has persistent fetal circulation (PFC) the oxygen requirement increases rapidly the further the pH is below 7.45. The oxygen requirement also fluctuates rapidly, simulating shunting. The P_{O_2} depends on the following parameters:

- Decreases if PIP is so high that it cannot be reached during the allowed IT;
- Decreases if the IT is less than ideal;
- Decreases if PEEP is below the ideal;
- Decreases if PEEP compromises blood return to the heart;
- Decreases as the tidal volume (TV) decreases;
- Decreases if the TV is less than ideal;
- Does not increase significantly if TV is greater than ideal (TV is correlated with PIP minus PEEP);
- Decreases with insufficient suctioning, stomach decompression, checking of the ET tube position;
- Decreases when fluid overload causes congestive heart failure;
- Decreases with a decreased F_{iO_2};
- Decreases with worsening disease (from oxygen array);
- Decreases with increased P_{CO_2};
- Will not be lower than 5 mm Hg; and
- Has a random factor of up to 10% for each calculation.

Carbon dioxide array. This is similar in concept to the oxygen array. As a disease worsens, more ventilation is required to keep the CO_2 within an acceptable range. If a patient has pneumothorax, then the ventilatory requirement increases with each successive six hours. If the patient has PFC, the ventilatory requirement increases rapidly the further the pH is below 7.45. The ventilatory requirement also fluctuates rapidly, simulating shunting. The level of CO_2 changes as indicated under the following conditions:

- Increases if expiratory time is <0.4 seconds;
- Increases if PIP is so high that it cannot be reached during the allowed inspiratory time;
- Increases if PEEP is below the "ideal" PEEP;
- Increases if PEEP compromises blood return to heart;
- Increases with decreased TV (TV is correlated with PIP minus PEEP);
- Increases with insufficient suctioning, stomach decompression, checking of the ET tube position;
- Increases when fluid overload causes congestive heart failure;
- Increases with decreased RR;
- Increases with worsening disease (from CO_2 array);
- Will not exceed 400 mm Hg; and
- Has a random factor of 10% for each calculation.

PIP array. This is a linear model of the ideal peak inspiratory pressure for an infant at any time during a disease. This array is used to evaluate efficacy of ventilator settings at all times during the program. Larger infants have higher ideal PIPs. Ideal PIPs range from 15 to 29 mm Hg, depending on the size of the infant and the state of the disease.

The following is an illustration of the set of guiding comments that are displayed if the student chose the elementary level of instruction. If PIP<1, DM = "One cannot provide a PIP in the range you requested," If PIP≤PEEP, DM = "In combination with the PEEP, this PIP will produce zero tidal volume." If PIP>79 mm Hg, DM = "One cannot mechanically obtain a peak pressure that high." If the P_{CO_2} is in a satisfactory range and a rapid change in PIP is requested, DM = "The PIP change you are planning in not cautious. Unless you have very good reasons, the PIP change should not exceed 10% of the previous PIP value." If PIP is decreased, DM = "The difference between PIP and PEEP determines the tidal volume. Does your lowering of PIP reflect a wish to lower the tidal volume with a resulting decrease in oxygenation and ventilation?" If PIP is increased, DM = "The difference between PIP and PEEP determines the tidal volume. Is your increasing of PIP testing the hypothesis that you are currently underventilating the baby?" If an increase in PIP helps the baby approach the ideal PIP-PEEP, then DM = "You are making a reasonable move. This baby may very well be underventilated and this increasing of the PIP will increase the tidal volume." If a lowering of PIP helps the baby approach the ideal PIP-PEEP, DM = "Tidal volumes higher than necessary are not useful and might actually be dangerous. Lowering the PIP in this situation is quite likely to have minimal effect on ventilation and oxygenation." If PIP is increased over 25 mm Hg, DM = "Remember: the higher the PIP the more likely you are to cause pnuemothorax and other pressure related trauma such as bronchopulmonary dysplasia in the long run." Changing PIP and obtaining a new blood gas analysis takes 30 minutes on the programs's time scale. At the more sophisticated, comment-free mode, the learner may infer the consequences of poor decisions only by their detrimental effects on the patient's status.

PEEP array. This is similar in concept to the PIP array. The ideal positive end expiratory pressures for infants with RDS range from 2 to 7 mm Hg, depending on the size of the baby and the state of the disease. For infants with PFC the ideal PEEP is near zero. If the RR is greater than 60, the ideal PEEP becomes progressively lower. A number of restrictions and warnings are displayed at the elementary level of instruction on invoking a change in PEEP. In general, if PEEP is lowered, DM = "By lowering PEEP you are stating that the PEEP was not needed at

the current level to maintain open airways at the end of expiration. You are also increasing the tidal volume." If PEEP is increased, DM = "By raising PEEP you are not only attempting to open up the airways that were previously collapsing at the end of expiration, but you are also making the tidal volume smaller, which will decrease ventilation." If PEEP<2 mm Hg, DM = "A PEEP that low is unobtainable on this ventilator." If PEEP≥PIP, DM = "A PEEP that high is greater than the PIP and gives a tidal volume of zero." If PEEP>14 mm Hg, DM = "The respiratory therapist points out that you have asked for a very elevated PEEP. It is unusual to require a PEEP that high." If PEEP<3 mm Hg and the baby does not have PFC, DM = "A PEEP that low is sub-physiological and is not good medical practice." If PEEP is changed more than 2 mm Hg at a time, DM = "It is dangerous to change PEEP more than a little at a time." If PEEP is very high, DM = "Your PEEP is at a level high enough to impede venous return to the heart and to cause overdistension of the alveoli; this will compromise this baby's circulatory and ventilatory status." If PEEP is increased and is much less than ideal, DM = "It is reasonable to raise PEEP in the current situation." If PEEP is decreased and is much greater than ideal, DM = "It is quite reasonable to lower PEEP in the current situation." As with other ventilator responses, changing PEEP and obtaining a new blood gas analysis takes 30 minutes on the program's time scale.

These two sets of comments regarding changes in PIP and PEEP illustrate the additional instructional functions of the program. They teach or remind the student of the rationale and consequences of his actions or omissions.

Physical examination array. This array provides a number between 1 and 4 indicating the severity of disease. The higher the number, the more severe the disease state. These numbers are used to provide appropriate results of physical examinations when requested.

Heart rate increases under the following conditions: with low infant weight; with hypovolemia or hypervolemia; with increasing temperature; with worsening disease; by up to 10 beats/min randomly; and to over 190 beats/min with pneumothorax. At no point should heart rate exceed 205 beats/min. Systolic BP increases with increasing weight, over the first 2 days of life, and with hypervolemia. However, it decreases by up to 15 mm Hg randomly with hypovolemia, with worsening disease, and with pneumothorax. At no point should systolic BP fall below 10 mm Hg.

If suction, stomach decompression, or checking the ET tube is inadequate, or if the P_{CO_2} is greater than 70 mm Hg, DM = "Decreased breath sounds bilaterally." If lack of suctioning, stomach compression, or neglecting the ET tube status causes severe effects on the infant's condition, DM = "Very faint breath sounds bilaterally." If there is pneumothorax, DM = "Decreased breath sounds unilaterally." If none of the previously mentioned occur, DM = "Good breath sounds bilaterally."

There are five different messages that are displayed according to the level of PIP, PEEP, and attention to suction, stomach decompression, and ET tube positioning. The higher the PIP then the larger the chest excursion will be. The higher the PEEP, and the less attention given to the latter three factors, then the chest excursion will be smaller. Adequate chest excursion occurs when the user approximates the ideal PIP and PEEP as calculated in their respective arrays. The DMs are: "Very large chest excursion on inspiration," "Large chest excursion on inspiration," "Good movement of the chest wall on inspiration," "Small chest excursion on inspiration," and "Chest excursion is barely seen upon inspiration."

When pneumothorax occurs, DM = "Assymmetry is evident: the right chest moves more than the left." (The programmed pneumothorax always occurs on the left.) If a chest tube has been inserted, DM = "A chest tube is secured in the left chest."

Urine output increases the less the baby weighs, increases with hypervolemia, and increases when the RDS begins to improve, and it decreases with hypovolemia. Urine output should not exceed 36 cc/kg/4 h and is 0 cc/kg/h for up to 18 hours after birth. If urine output has been 0 since birth, DM = "No urine output since birth. (Infants often do not urinate prior to 24 hours of age.)" If urine output has been 0 cc for four hours, DM = "There has been no urine output during the past four hours." If there has been urine output over a certain time period, then the display will reflect that change.

The temperature is displayed as a random number between 97.5°F and 99.5°F. If the temperature is greater than 99.3°F, DM = "The nurse says that the warming table is too hot."

Since the patient is on a ventilator all physical examinations, DM = "There is no spontaneous respiratory response."

A physical examination may be completed in 12 minutes on the time scale of the program. If the physical examination has just been done, DM = "The physical exam findings have not changed since previous examination."

Chest radiography array. Depending on the chest radiography array (scored 1 to 5), DM = (1) "Slight diffuse granularity throughout all lung fields;" (2) "Mild diffuse granularity throughout all lung fields;" (3) "Moderate diffuse granularity throughout all lung fields;" (4) "Severe diffuse granularity throughout all lung fields;" or (5) "Complete white-out of both lungs."

If pneumothorax is present (always on left), DM = "Absence of lung markings on the left; heart shifted to the right." If a chest tube has been inserted recently, DM = "Chest tube in left chest. No evidence of pneumothorax." If a chest tube was inserted a long time ago, DM = "Chest tube in left chest. Improving clarity of lung fields." If pneumothorax is present and a physical examination performed and a radiogram requested before chest tube insertion, DM = "If a suspected pneumothorax is real, the baby can get much sicker during the time elapsed while waiting for the x-ray. Do you still want to order the x-ray?" An x-ray procedure takes one hour on the program's time scale.

Check ET tube array. This array evaluates the student's attention to this factor (scored 0 to 3). If the user requests this option the array is set at 0. If the user does not request this option, there is a 2% chance per hour that this array will be incremented by one point. If the ET tube array variable is 0, DM = "The ET tube was clear and in good position." If the ET tube array variable is 1, DM = "The old ET tube was slightly obstructed. The plug was re-

moved." If the ET tube array variable is 2, DM = "The old ET tube was moderately obstructed. The plug was removed." If the ET tube array variable is 3, DM = "The old ET tube was plugged. The ET tube was changed." On the computer's time scale it takes one hour to complete this procedure and obtain a new blood gas analysis.

Complication. VSP can present the student with the following five complications. (1) The likelihood of pneumothorax increases with increasing PIP and PEEP, overventilation as reflected by a falling P_{CO_2}, and with a longer IT. When pneumothorax occurs it is reflected by worsening blood gases and a changing physical examination. It is also shown on radiographic examination. The user must request a new physical examination or radiography before this information is provided. (2) "A dramatic rise in the lungs' circulatory shunting due to alveolar hypoxia" occurs if the P_{O_2} falls too low and is reflected by a major worsening in the patient's ventilatory status. (3) If the PEEP is too high, or the patient is either volume-depleted or overloaded, then the patient's circulatory status is compromised and an increasing acidosis and worsening ventilatory status manifest. (4) Congestive heart failure occurs if the patient is consistently hypervolemic for longer than six hours. Congestive heart failure influences the infant's respiratory status. (5) Finally, if sufficient insults have occurred due to the inability to attain a stable status, the baby will "die."

Bystanders. As teaching aids, the program has four bystanders—the Nurse, the Authority Figure, the Good Doctor, and the Death Angel who intervene under particular circumstances. If the user has requested the WAIT option, then the Nurse is alerted. If during the waiting period the pH falls below 7.25 or rises above 7.60 or if the P_{O_2} falls below 40, then the Nurse interrupts the wait period with the following: DM = "The nurse asks you to see the baby immediately because the baby has worsened and questions whether an x-ray is in order. If insufficent suctioning has been done, DM = "Do you think we should suction the baby?" If insufficient stomach decompression has been done, DM = "Do you think it would help to decompress the stomach?"

Every midnight an Authority Figure "checks" on the patient's progress and comments if the pH is less than 7.25 or greater than 7.55. One of the following three messages selected at random is then displayed: "Attending nails you to the wall in the morning;" "Visiting attending cringes noticeably on rounds;" or "Your senior resident stomps all over you." The following solutions are then offered: "Have you tried raising the RR?" "Have you raised the PIP enough?" "Is your PEEP too high or too low?" "Is your E-time sufficient?" "Have you given enough fluids?" "Have you tried lowering the RR?" "Have you lowered the PIP?"

The Good Doctor is waiting to discontinue the patient's pancuronium bromide if the case has been managed successfully to the point that the infant no longer needs the ventilator. The Good Doctor looks at the following factors in his evaluation: If the P_{O_2} is greater than 55, the P_{CO_2} less than 40, the F_{iO_2} less than 0.4, and the RR less than 23, then the criteria for reversing the baby's paralysis are met. However, the Death Angel keeps track of insults that the patient has sustained during the case. If the patient has been sick enough during the program, death will result. The following factors are evaluated by the Death Angel every hour: pH, P_{O_2}, volume status, and magnitude of PIP. If the patient dies the Death Angel interrupts the case and the program goes through the Stop & Score routine.

Stop and Score routine. This may be initiated either by user request or when the program determines that the patient is either well on his way to recovery or has died. In scoring the student's performance (Fig 4), VSP evaluates how closely the patient's management approximated the goals outlined at the outset. Scoring is done on a scale of 100 to 0. During case management points are deducted for allowing the pH to run too high (>7.45 for RDS, >7.55 for PFC) or too low (<7.26 for RDS, <7.36 for PFC); the further the pH is from the ideal, the more points are deducted. Allowing the P_{O_2} to run too high (>100 for RDS, no limit for PFC) or too low (<50 for RDS, <100 for PFC) also causes points to be deducted. Points are deducted for pneumothorax occurrence secondary to poor ventilator settings, for causing congestive heart failure due to poor fluid management, or for chest tube insertion without prior physical examination. At the end of a case, points are deducted for the following: the death of the patient; not treating pneumothorax; having a completely plugged ET tube; giving the patient too much or too little fluid; running the PIP or PEEP significantly above ideal; not doing a physical examination within the first six hours from arrival or not doing a daily physical examination; for taking too many radiograms; and for checking too many blood gases (more are allowed the sicker the patient becomes).

Figure 4 is an example of a score feedback message display. Some messages displayed when applicable include the following: You took too many x-rays; you should have taken an x-ray; you should have done a physical examina-

```
You managed this patient for 1 day.

THE PATIENT DIED DUE TO RESPIRATORY INSUFFICIENCY.
THERE WAS A SIGNIFICANT COMPONENT OF CONGESTIVE HEART FAILURE SECONDARY TO
FLUID OVERLOAD WHICH CAUSED 'FLOODING' OF THE LUNGS.

YOUR SCORE WAS  15/100.

For blood gases you spent $ 260
For chest X-RAYS, you spent $ 296

YOU SHOULD HAVE DECOMPRESSED STOMACH MORE.
YOU DIDN'T DISCOVER THE PNEUMOTHORAX.

RANKING: INTERN CLASS.

Would you like to see a listing of the Blood Gas Summary? ▮


You managed this patient for 3 days.

YOU'VE MANAGED THE PATIENT SO WELL THAT HE CAN COME OFF PAVULON!
YOUR SCORE WAS  97/100.

For blood gases you spent $ 702
For chest X-RAYS, you spent $ 148


RANKING: NEONATOLOGY ATTENDING LEVEL.

Would you like to see a listing of the Blood Gas Summary? ▮
```

FIGURE 4. Typical final report displays.

Baby Boy Bigelow — BLOOD GAS SUMMARY — PAGE 3
1.8 kg at birth

DAY	HOUR	FiO2	RR	PIP	PEEP	I-TIME	PH	pO2	pCO2	HCO3
2	12:40	0.35	26	23	3	0.9	7.36	53	43	23
2	13:10	0.35	26	24	3	0.9	7.38	57	38	22
2	13:40	0.38	26	24	3	0.9	7.39	66	37	22
2	17:40	0.38	26	24	3	0.9	7.36	81	37	20
2	23:40	0.38	26	24	3	0.9	7.37	74	33	18
3	0:10	0.38	26	24	3	0.9	7.41	90	30	18
3	0:20	0.38	26	24	3	0.9	7.42	77	30	19
3	0:40	0.38	26	24	3	0.9	7.44	85	28	18
3	1:10	0.38	26	24	3	0.9	7.52	89	24	18
3	1:40	0.38	20	24	3	0.9	7.44	88	31	20
3	2:10	0.38	20	22	3	0.9	7.43	87	33	21
3	2:20	0.38	20	22	3	0.9	7.39	77	36	21

Do you want to (1) Quit or (2) See another page: ▮

FIGURE 5A. Typical page display of the "Blood gas summary."

tion on a certain day; you should have suctioned more often; you should have decompressed the stomach more, you need to check your ET tube position more often; and you should have given more fluid or you gave too much fluid.

The method of scoring after completion of the simulation is as follows: 0 to 29, intern; 30 to 59, senior resident; 60 to 89, fellow; and 90 to 100, neonatology attending. At the end of the score routine the student has the option of receiving a printout that summarizes the sequence of blood gas status throughout the management period. This allows for a self evaluation or reassessment of the management in consultation with others. Figure 5 is an example of such a report.

Experiences and Projections

House officers who have used this simulator both in Boston and in Buffalo have expressed enthusiasm for it. They felt that it allowed them to test their knowledge and also to learn new options for ventilating infants. Some pointed out that with emphasis on checking the ET tube position, maintaining a clear airway, and stomach decompression the program reminded them how important these maneuvers are in an actual situation. Those who had previous experience with ventilated infants felt that the program effectively simulated an infant with RDS. In Buffalo, this program was given to junior medical students in conjunction with a course on the use of monitors in intensive care. The program was run by groups of two or three students who had minimal experience in intensive care. The students appeared fascinated by the program and exercised with it for hours, recalling their previous education in basic physiology and pathophysiology. The students discussed the appropriate action in a given situation; these discussions may have been as instructional as running the program itself. Following such a simulator exercise the researchers found that one could more effectively discuss with a whole class the different aspects of intensive care and respiratory problems. It seems therefore that such simulators could be introduced earlier in medical education, providing students with the opportunity to care for simulated critically ill patients.

From the short experience—approximately two years—of providing this program to both students and house staff, it is difficult to assess objectively the long-term effects of this instructional experience on clinical practice in neonatology. The researchers found that the users improved their performance on the simulator as they practiced with it. At present a comparative study is being conducted in Buffalo on the performance of users who have been exposed to this type of computer-based instruction. However, it will take several years before sufficiently reliable data become available. In the meantime favorable conclusions may be drawn only by analogy by using nonmedical experiences where rapid response to complex multiparameter controlled situations are called for: the successful use of flight simulators, simulators of nuclear reactor control, and electronic "sand boxes" in the training of military personnel. What has been shown here is that a similar level of reality may be simulated by computers in medicine as well.

It has been stated that computer based instruction, including the use of clinical simulations, may not be as cost effective as classic teaching methods.[27] This may also be true of multiple choice programs in view of the programming effort involved compared with the traditional dissemination of the same material.

VSP is an example of a computerized simulation of a complex patient management problem. Managing a patient implies understanding the underlying pathophysiology of that particular patient. In the past, attention has been given to diagnostic problems that may not always require a dynamic multiparameter analysis. However, in intensive care or in similar situations in medical practice far more time is devoted to the management of a pathologic process than to its diagnosis. Further, since management involves control of the patient's status while finding optimal methods of treatment, it presents far more intellectual challenge.

```
You managed this patient for 5 days.

YOU'VE MANAGED THE PATIENT SO WELL THAT HE CAN COME OFF PAVULON!
YOUR SCORE WAS  68/100.

For blood gases you spent $ 1170
For chest X-RAYS, you spent $ 148

YOU SHOULD EXAMINE THE PATIENT MORE OFTEN ON THE FIRST DAY OF LIFE.
YOU GAVE TOO MUCH FLUID.
YOUR LAST PIP WAS TOO HIGH FOR THE BABY'S RESPIRATORY STATE AT THAT TIME.

RANKING: FELLOW LEVEL.

Would you like to see a listing of the Blood Gas Summary?
```

Baby Boy Jones — BLOOD GAS SUMMARY
2.2 kg at birth

DAY	HOUR	FiO2	RR	PIP	PEEP	I-TIME	PH	pO2	pCO2	HCO3
1	1:00	0.75	24	21	4	1.5	7.31	178	45	21
1	1:30	0.50	24	21	4	1.5	7.31	131	44	21
1	2:00	0.40	24	21	4	1.5	7.31	105	45	21
1	2:30	0.40	24	21	4	1.0	7.30	94	48	22
1	3:30	0.40	24	21	4	1.0	7.32	92	44	22
1	7:30	0.40	24	21	4	1.0	7.24	87	55	23
1	8:00	0.40	30	21	4	1.0	7.29	78	46	21
1	8:30	0.40	30	21	4	1.0	7.34	93	38	19
1	12:30	0.40	30	21	4	1.0	7.32	98	41	20
1	12:40	0.40	30	21	4	1.0	7.31	95	41	20
1	16:40	0.40	30	21	4	1.0	7.36	93	41	22
1	20:40	0.40	30	21	4	1.0	7.30	78	49	23
1	21:10	0.40	30	21	4	1.0	7.37	94	40	22
2	3:10	0.40	30	21	4	1.0	7.26	79	51	22
2	3:40	0.40	30	21	3	1.0	7.31	77	47	23
2	6:40	0.40	30	21	3	1.0	7.21	58	58	22
2	7:10	0.40	30	23	3	1.0	7.24	59	53	22
2	7:40	0.40	30	23	3	1.0	7.30	81	43	20
2	7:50	0.40	30	23	3	1.0	7.37	90	38	21
2	8:00	0.40	30	23	3	1.0	7.31	87	42	20

FIGURE 5B. Typical printout of a final report and part of a summary.

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INFANT RESUSCITATION

The first requisite in resuscitation of the apneic newborn is the establishment and maintenance of a free airway. External stimulation may then be tried. The major point to be emphasized with such stimulation is gentleness; the risk of causing visceral trauma, increased shock, and cerebral hemorrhage is very real. Oxygen is to be administered and warmth maintained. Utilization of technics of artificial respiration such as endotracheal intubation and insufflation requires a considerable amount of training and a high degree of practical skill. Considering the ease with which the newborns tissues may be traumatized and the respiratory distress increased rather than relieved, such technic should be performed only with great care and gentleness despite the urgency of the situation.

We have found that the best results parallel the cooperation and coordination of the obstetric, pediatric, and anesthesiology departments. Coordinated training and standardization of technics of resuscitation are prime requirements in the successful handling of respiratory difficulties in the newborn.

H. D. EASTMAN, MD
(*NY State J Med* 1948; 48: 707)

The Great Biologic Problem:

Vitalism, materialism, and the philosophy of organism

JOHN S. HALLER, JR

All are but parts of one stupendous whole,
Whose body Nature is and God the whole.
Alexander Pope

All our poetry, all our science, all our art, Plato, Shakespeare, Newton, and Raphael, are potential in the fires of the sun.
John Tyndall

In 1907, an article appeared in *American Medicine* that not only evoked a storm of controversy among professionals within the sciences, but had wide audience in the popular press as well. The author, Duncan MacDougall, MD, of Haverhill, Massachusetts, suggested that upon death a material, space-occupying "soul substance," essential to the body in life and a form of "gravitative matter," leaves the body and enters the earth's ether. MacDougall speculated that the earth, in its movement through space, carries a layer of ether many times its own size. The ether constituted "a real world above the storm zone of the earth's atmosphere . . . [of] beings constituted entirely different from us, who are yet subject to gravitation." It was there that the spiritual principles of human beings continued to exist after death. Since these spiritual principles were not subject to gravitation, "it follows that ever since human beings began to die upon the earth, the complex pathway of the earth around the sun in space, and of the earth as part of the solar system moving in space, is littered with these non-gravitative spiritual principles."[1,2]

This hypothesis of existence after death was less satisfying than the more traditional belief in physical resurrection; however, it did imply a mode of survival that MacDougall believed verifiable by close investigation at the moment of death. "The essential thing," he wrote, "is that there must be a substance as the basis of continuing personal identity and consciousness, for without space-occupying substance, personality or a continuing conscious ego after bodily death is unthinkable."[1]

Although MacDougall's theory appeared unorthodox to many of his colleagues, the elements from which he drew his thesis were part of western civilization's earliest oral and written traditions. In fact, his "soul substance" was but the newest entry into the fundamental debate in medicine and the basic principle in all biology (ie, "What is Life?"). The quest among scientists, physicians, and philosophers to identify the activities or forces dominant in organic processes became known as the Great Biologic Problem, named for the literature dealing with the age-old debate between the opposing schools of vitalism and materialism. MacDougall's assertion for the materiality of the soul was but an extension of the argument for a "special soul substance," first proposed by physiologist Rudolph Wagner at the Gottingen Congress of Physiologists in 1854. Like so many before and after him, MacDougall had crafted a theory containing arguments as old as the most ancient philosophers and as modern as the newest science fiction novel.[3-7]

The medical profession found itself very much in the middle of this debate out of fear of being "led into false beliefs which will be injurious to our patients."

> It may seem a far cry from a discussion of what is life to what to do for a typhoid case, yet every single remedial measure is directed toward a vital phenomenon; consequently, common sense dictates that we should learn what is meant by the word "life," for we should not be ignorant of the very thing occupying our whole time. Prolongation of human life is the sole purpose of our professional existence, and it certainly behooves us to know what we are prolonging.[8-10]

Indeed, physicians understood that the modus operandi of remedial agents depended on how the nervous power, the soul, and the principle of instinct related to the vital principle. All stimuli, whether natural, morbific, or remedial affected the body through the vital properties; disease consisted of a modification of those properties and a resulting change in function. "Disease," wrote Martyn

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Paine (1794 to 1877), "is essentially nothing more than a deviation of the properties of life from their natural standard, and a consequent corresponding change of functions over which the affected properties preside."[11-13]

Early Years of Debate

The conception that living bodies possess within themselves an active force that differs from anything possessed by nonliving matter was the starting point for the theory of vitalism. The origins of the philosophy of organism precede written history and may be found in the animism of the earliest cultures, that held that the spirit of a ghost inhabited the living body and was responsible for its actions. During the course of a disease, this spirit was thought to have been dispossessed by a more evil spirit. Eventually, vitalistic theories that contained expressions of life's "why" and "how" commingled with the systems of theology, metaphysics, and natural science in a variety of ratiocinations.

For vitalists, life represented a new and foreign principle or substance imposed on the materials that constituted the body. Some individuals saw this as little more than activating forces latent in the materials themselves while others implied the existence of a "soul," or something fully external that acted on the body. Despite their different approaches, life always had a dynamic element that remained inaccessible to human understanding despite known laws governing the organic and inorganic worlds. Through most of its history, vitalism was a philosophic concept independent of natural science.[14]

The early Greeks endowed water, fire, and earth with the life-creating principle. The philosopher, physician, and poet Empedocles (504 to 443 BC) of Agrigentum in Sicily, asserted that living beings formed by the chance union of reckless bodies, legs, and other parts were shaped by Strife or Love and the mutual attraction and repulsion of the four basic elements. Although Anaxagoras of Clazomena (500 to 428 BC) believed that the living body was formed from a primitive matter composed of the elements of water, fire, and earth and endowed with Mind, or nous, Hippocrates (460 to 377 BC), who gave to Greek medicine its scientific spirit, ascribed the essence of life to ether, a subtle fire existing from all eternity and present in air and all matter. This ether was identical with the pneuma described elsewhere in the works of Plato (427 to 344 BC) that were the authoritative doctrine for nearly 15 centuries. To some, the pneuma had the attributes of a material substance comparable to oxygen; to others it was an intangible concept theoretically essential to the understanding of life. In any case, it was certainly antecedent to MacDougall's speculations more than two thousand years later.[15-19]

Aristotle (384 to 322 BC), Plato's pupil, contributed to modern physiologic doctrine by listing the attributes of growth and decay, nutrition and reproduction, and the capacity for responding to stimuli as elements that composed a living body. In *The History of Animals* and *Concerning the Soul*, he established a medico-philosophic position that would exist through the Middle Ages. Dissatisfied with a purely mechanical explanation of life and anxious to wrestle with the rationality of existence, Aristotle made the distinction between the potentiality of matter and the actuality of form; all substances arose from a combination of the two. In effect, Aristotle occupied a middle ground between the idealism of Plato and the purely mechanistic doctrines of Democritus.[20-25]

For those of the Hippocratic school, the ether, immortal spirit, or pneuma entered the body through the lungs and, carried throughout the body in the blood, sustained vital action or life force. By 300 BC, the Alexandrians had divided this force into two separate agents: the vital spirits that resided in the heart, and the animal spirits that resided in the brain.[26-27]

Claudius Galen (131 to 200 AD), building upon the pneumatic theories of Athenaeus, Aretaeus, and Archigenes, recognized the importance of anatomic research in comprehending physiologic function and life. Galen added yet another force to the two identified by the Alexandrians—that of natural spirits that resided in the liver. According to Galen venous blood, originating in the liver, traveled to the right side of the heart where a separation took place: the living portion proceeded to the left side of the heart and the dead portion moved to the lungs where it underwent refreshment under the influence of the life-giving pneuma. His writings, based on Greek biologic specu-

FIGURE. Paracelsus, 1493 to 1541. Portrait engraved by Romeyn de Hooghe (1645 to 1708).

lations grafted to Roman thought, influenced many successive generations of scientists and physicians.[28-33]

Eventually, the doctrine of the pneuma evolved into the archeus of Paracelsus (1493 to 1541) and of the mystic Jan Baptista van Helmont (1577 to 1644), and the anima sensitiva of pietist Georg Ernst Stahl (1660 to 1734) of Ansbach in Bavaria. Paracelsus, who initiated a drug-induced search for the elixir or quintessence of all things, believed that Mosaic creation necessitated the pre-existence of the archeus, a force that governed the chemical processes of the body. To him, this force had a double nature: a visible or earthly side and an invisible or astral side. Both parts existed in everything living and lifeless. van Helmont completed Paracelsus' thought in his doctrine that the archeus along with matter was a universal component, diffused in varying proportions, and in all things. The archeus of van Helmont, which in some ways was an inferior edition of Aristotle's soul, presided over the human organism and governed its harmony in health and its disharmony during disease.[34-35]

Georg Stahl, the originator of the phlogiston theory in chemistry, restated this spiritual governing force some hundred years later by restructuring van Helmont's idea of the sensitive soul as the source of vital phenomena. "The events of the body may be roughhewn by chemical and physical forces," he wrote, "but the soul will shape them to its own ends, and will do that by its instrument, motion." Stahl's more chaotic conception of the vital force, explained in his *Theoria medica vera*, held that the body existed only for the soul which, living for its own ends and purposes, struggled against the physical and chemical activities threatening life.[36-37]

Stahl's vitalism in its extreme animistic form would emerge later in the dogmatic theory of Gottfried R. Treviranus (1776 to 1837), who argued that the soul employed the forces of the material world to form the organism. Although his outlook changed over the six volumes of his *Biologie, oder Philosophie der lebenden Natur*, Treviranus nonetheless stressed the instinctive or unconscious aspect of vitalism in contrast to the purposiveness inherent in the vitalism of Stahl.[38]

Opposed to vitalism in all its various forms was the conception of the living body as a mechanism. Although Galen's soul is certainly material or quasi-material, the modern form of mechanism first appeared in the physiology of Rene Descartes (1596 to 1650). In *Principles of Philosophy* (1644), Descartes accepted mechanism as the most satisfying metaphysical doctrine for the material world. He suggested that life was a mechanical process in which the soul did only what it was conscious of doing. For him, the body was little more than a machine.

> All the functions of the body follow naturally from the sole disposition of its organs, just in the same way that the movements of a clock or other self-acting machine or automation follow from the arrangement of its weights and wheels. So that there is no reason on account of its functions to conceive that there exists in the body any soul, whether vegetative or sensitive, or any principle of movement other than the blood and its animal spirits agitated by the heat of the fire which burns continually in the heart and does not differ in nature from any of the other fires which are met with in inanimate bodies.[39-41]

Between the materialism of Descartes and the external life force known as the soul were the ideas of Ralph Cudworth (1617 to 1688) and Francis Glisson (1597 to 1677), Regius Professor of Physic at Cambridge. Cudworth objected to Descartes' denial of the unconscious processes of the soul and the purely mechanical process with which he explained life. He suggested instead that a universal plastic matter, intermediate between God and the world, that was also immaterial, acted purposely but without will or reason. Found in every human and animal soul, this plastic matter bridged the gulf between mechanism and thought.[42] Glisson argued that everything that had substance and existence also had activity. The activity of life was inherent in both the spiritual and material forms. Matter, he wrote, "is not only capable of life but is also actually living."[28,43] Glisson, following Paracelsus, introduced the concept of irritability as the specific property on which the energy of living matter depended. Later William Hunter (1718 to 1783) would separate living and nonliving matter by suggesting a *materia vitae diffusa* to explain his physiologic and pathologic ideas.[44,45]

Another challenge to Cartesian materialism was by Gottfried Wilhelm Leibnitz (1646 to 1676) who replaced Cartesian dualism with the concept of the monad—an active, primitive, immaterial center of force brought into existence by God and existing in all matter. Leibnitz postulated that there was an inequality or hierarchy among the monads and that in living bodies, a central monad acted as the soul. Although the soul was not conscious of all its actions, it interacted with matter within a pre-established harmony.[46]

The gulf between living and nonliving matter narrowed in the 18th century, especially with developments in chemistry, physiology, and physics. Clearly the controversies that erupted between vitalists such as Stahl and the iatromechanical school established the need for a more experimental biology. While the theory of the soul faced harsh criticism, life now became a product of the organized matter itself; living matter carried with it an inherent material entity, a product of the physical body. Thus the 18th century became an age of clarification with the philosophies of John Locke, Voltaire, Julien Offrey de La Mettrie, and Leibnitz serving as stimuli to the labors of John Bernouilli, Luigi Golvani (1737 to 1798) of Bologna, Alessandro Volta, Joseph Priestley (1733 to 1804), Antoine-Laurent Lavoisier (1743 to 1794), Carl von Linnaeus (1707 to 1778), and Georges Leclerc Comte de Buffon (1707 to 1788). A believer in spontaneous generation, Buffon argued that disorganized organic particles arranged themselves under natural circumstances to produce living structures. Unlike the more radical materialists, however, Buffon shied away from any purely random process of creation. There was an internal fabric to the cosmos which assured that all life forms followed certain designs or structures.[47-54]

William Cullen (1710 to 1790), John Brown (1735 to 1788), and, through Brown, Benjamin Rush (1745 to 1813), Francois Boissier de Sauvages (1706 to 1767), Giovanni Rasori (1766 to 1837), and Francois Broussais (1772 to 1838) gave the issues of vital force an important new perspective in the 18th century. Throughout their extensive experimentation, these researchers maintained the existence of a force that defied complete definition. While

they accepted in principle the idea of vitalism, they found the unitary concept of Stahl's anima no longer entirely accountable for the phenomenon of life. For them, the vital principle became less of a centralized force governing the body; instead, they decentralized the principle within and among the isolated happenings in the body, such as the irritability of muscle or the sensibility of nerve. For Friedrich Hoffman (1660 to 1742), it became spasm and atony while Cullen viewed life as a function of nervous energy, Brown as stimulation, Rasori as stimulus and contrastimulus, and Broussais as irritation.[55-61]

Theophile de Bordeu (1722 to 1776), the founder of the vitalistic school of Montpellier, decentralized the anima by diffusing its properties throughout the organs of the body. Each organ has a *vita propria* presided over by the stomach, heart, and brain. John Christian Reil (1759 to 1813) of Germany, however, chose a more philosophic stance by positing an unknown force that arose from a novel combination of elements and that controlled the mechanical forces of the body.[28,62]

Albrecht von Haller (1708 to 1777) distinguished between muscular irritability and nervous sensibility and explained that physiology was in large part dependent on both elements. In doing so, Haller removed the deux ex machina that earlier physicians had postulated, replacing it with the physiologic principles of irritability and contractability. The achievements of Haller and Giovanni Morgagni (1682 to 1771), a professor at Padua, were due in part to the work of John Brown of Edinburgh, the modern representative of the first century Methodists who established a plan for stimulating or lowering the system with tonics and purgatives depending on whether the disease was sthenic or asthenic.[63-69]

Much of the thinking on vitalism changed with the patient work of Johannes Muller (1801 to 1858) of Coblenz, the father of modern physiology. Although he found Stahl's views congenial to his own, his understanding of vitalistic theory changed over the course of his inquiries; eventually Muller insisted that the principle of a force rather than an imponderable matter was basic to any explanation for the mechanisms of the living body. He believed that all matter contained, in latent form, both the vital and mental principles essential to living bodies. "The vital principle," he wrote, "is in a quiescent state in the egg before incubation." Nevertheless, he chose to explain life in mechanical terms; vital force "followed the lines of physical and chemical forces, however different it might be from these forces themselves."[28,70]

Johann Friedrich Blumenbach (1752 to 1840) provided an overview on the entire subject in two monographs: *Institutiones physiologicae* (1787) and *Uber den Bildungstrieb* (1789). Beginning with a historical sketch of past and contemporary thought on the subject, he then focused on his own vitalistic beliefs, arguing for an innate impulse for self development and reproduction in all living creatures. Blumenbach established the doctrine of vitalism on the basis of scientific rationalism.[71-72]

Nineteenth Century Developments

The philosophical debate of the 18th century between vitalism and materialism continued arguments that had troubled scientists and philosophers from earliest times. Issues involving distinctions between human beings and the rest of the animal world, and the ranked hierarchy of existence, were the basis of these arguments. Opinions varied on the precise point of discontinuity that "abruptly and fundamentally severs those bodies which have [a mental or spiritual life] from those which do not have it."[73] Descartes, for example, placed the break between men and other animals; he considered animals as without souls and devoid of sensation and feeling. Lamarck, a materialist who believed that life was derived from matter by spontaneous generation, placed the discontinuity between worms and insects, using the presence of a nervous system as his criterion. Philosophers and natural scientists of the 19th century, on the other hand, placed the discontinuity even earlier in the chain (ie, at the very threshold between organic and inorganic material).[74-77]

In the early decades of the 19th century, discussion of the vital principles continued to intrude upon the thinking of physiologists. Writing in the *Transactions of the Royal Society of Edinburgh*, William Pulteney Alison, MD (1790 to 1859), professor of the practice of medicine at the University of Edinburgh, maintained the existence of a "power peculiar to living bodies" that he identified as "vital affinity"; this power was one of the first principles of physiology and pathology and equal in importance to the laws of motion or gravitation. There was no question in Alison's mind that vital affinity explained the various "attractions," "repulsions," and activities "peculiar to the living state."[78-80]

Alison held three propositions for explaining the introduction of living bodies into the world. First, he proposed that the earth existed before the creation of organized beings; secondly, the vegetable kingdom existed prior to the animal kingdom and "lived chiefly on the atmosphere, fixing large quantities of carbon from it on the earth's surface"; and third, that "the first living being of every species, vegetable and animal . . . must have been formed in a manner strictly miraculous, and . . . beyond the limits of physical science." Having been endowed at some critical point by the "Great Ruler of the universe," with the power to act on inorganic matter and extract from it the materials needed for growth and sustenance, species were then capable of perpetuation.[78]

By the middle of the 19th century, however, two discoveries forced considerable rethinking regarding the Great Biologic Problem. The first discovery was Robert Mayer's and James Prescot Joule's physical principle of the conservation of energy, demonstrated in 1842. Applied to the fields of chemistry and physics by Herman von Helmoltz (1821 to 1894) in 1847, it seemed to have left little room for a speculative vital force. The second discovery was Charles Darwin's (1809 to 1882) theory of natural selection that explained how something purposively constructed could arise by absolute chance. Adaptation became the aim of evolution, one derived from blind natural processes. These discoveries brought to the debate a tone more mechanistic than that of the iatrochemical and iatrophysical schools.

Advances in organic chemistry, the establishment of the law of conservation of energy, and the successful application of physical and chemical laws to life encouraged the conviction that "all life phenomena are nothing else

but complex phenomena of the inorganic world" and that there was no distinction between animate and inanimate phenomena. This mechanistic approach insisted that every aspect of life was capable of analysis by the methods of science. Enthusiasts such as Carl Vogt (1817 to 1895) even suggested that ideas were secretions of nerve cells. Others argued that there was little difference between the nerve cells that secreted ideas and the kidney epithelium that secreted urine. Thus while some insisted on the existence of a special vital principle in the living body independent of chemical forces, many other 19th-century thinkers were attempting to bury the claims of vitalism.[28,81-82]

Resurgence in materialistic thinking had been aided by morphologist Ernst Haeckel (1834 to 1919), Jacques Loeb (1859 to 1924), and Henry C. Bastian (1837 to 1915), whose *Beginnings of Life* (1872) attempted another revival of the theory of spontaneous generation. Bastian attempted to show that vital force was nothing more than a "specialized exhibition" of physical and chemical phenomena; physiology became applied chemistry and physics. From the beginning to the very end, the process of life entailed "no other guiding influence than the laws of the inorganic world." Any complexity resulted from the natural process of evolution and only vanity prevented vitalists from recognizing this mechanistic process.[83-95]

Just as Darwin had demonstrated the continuity between man and the rest of the animal kingdom, so Darwinists in the late 19th century attempted to prove that the vital principle could be discarded like the phlogiston theory in chemistry and the Ptolemaic theory in astronomy. "Henceforth," wrote John Fiske in his *Outlines of Cosmic Philosophy*, "the difference between a living and a not-living body is seen to be a difference of degree, not of kind—a difference dependent solely on the far greater molecular complexity of the former." Under favorable circumstances, there was nothing to prevent nonlife from becoming life. Fiske identified with Bastian's archebiosis as the most appropriate explanation of this process—a term more satisfying to him than spontaneous generation.[96]

The cellular doctrine emerged at the same time the vitalists were struggling with the materialists. Linked with this doctrine was the idea that protoplasm was the living substance of the cellular unit. Against the backdrop of the humoralists, with their mixture of blood, phlegm, yellow bile, and black bile, and the solidists with their nervous tissues, Rudolph Virchow's (1821 to 1902) *Cellular Pathology* explained the cellular nature of organized life forms with his dictum, "omnis cellula e cellula," meaning that every cell arises only from an already existing cell.[26,97-99]

For Virchow, the founder of cellular pathology, the search for the unity of life would remain a futile endeavor until those debating the issue recognized that highly organized life forms "were in reality organisms, each constituent part of which had its special life." This meant accepting the fact that "every living organism, like every organ and tissue, contains cells," and that "the cells are composed of organic chemical substances, which are not themselves alive." Virchow believed that Theodor Schwann's (1810 to 1882) cellular theory that established the existence of "free cell-formation," had in fact retarded the recognition of these factors. Schwann's theory of cytoblastema, rivaling the older doctrine of spontaneous generation, found sanctuary in the idea of the formation of plastic exudates. Virchow's experiments, however, proved otherwise. Virchow's influence maintained the vitalistic argument amid the pressures of late 19th-century materialism.[55,100]

> I myself was taught the discontinuity of pathological growths—a view which would logically lead back to the origin of living from non-living matter. But enlightenment in this matter came to me. At the end of my academical career I was acting as clinical assistant in the eye department of the Berlin Hospital, and I was struck by the fact that keratitis and corneal wounds healed without the appearance of plastic exudation, and I was thus led to study the process of inflammation in other non-vascular structures, such as articular cartilages and the intima of the larger vessels. In no one of these cases was plastic exudation found, but in all of them were changes in the tissue cells. Turning next to vascular organs, and, in particular, those which are common seats of exudation processes, I succeeded in demonstrating that the presence of cells in inflammatory exudates was not the result of exudation, but the multiplication of pre-existing cells.[44]

For many scientists in the late 19th century, the argument had narrowed to the proper understanding of cellular activity. It was there, the vitalist felt, that the mechanist's argument ultimately failed. The mechanist believed that a complex intracellular process, acting on purely chemical and physical lines, performed all the functions of the cell and that a full explanation of this process would, in time, become evident. These mechanisms or processes, they argued, were contained entirely in the nuclei of the ovum and spermatozoon and, through them, transmitted to successive generations. August Weismann (1834 to 1914) of Frankfort identified the substance as germ plasm. For the vitalist, however, this explanation was as incomplete as that of Emil Du Bois Reymond (1818 to 1896) who reduced all matter to the motion of atoms. It was erroneous, they argued, to explain one process by the introduction of yet another process. "We have, then, to proceed along mechanistic lines in chemistry and physics as far as possible, and where these sciences bring us to an impasse, the prominence of the failure will lead up to the vitalism of the future."[83,101-103]

The decades immediately following the publication of Darwin's *Origin of Species* precipitated a rash of materialistic theories that focused on the possibility of spontaneous generation. In the late 1880s, however, chemistry, physiology, general biology, and medicine saw a form of "neo-vitalism" surface in the works of embryologist Wilhelm Roux (1850 to 1924) of Halle and Eduard Rindfliesch, who claimed to be independent of the older schools of vitalism. Others among this group included the bacteriologists Paul Ehrlich (1854 to 1915), Hans Buchner (1850 to 1902), and Clemens von Pirquet (1874 to 1929); and among the clinicians, August Bier (1861 to 1949). These neovitalists hoped for a revival of teleology arising from what they had hoped would be the critique and fall of Darwinism.[104-106]

Much of the neovitalistic literature that continued into the 20th century was of German origin and expressed an uncompromising opposition to the French materialism of

the previous century. Foremost among the new school of neovitalism was Hans Driesch (1867 to 1941), professor of philosophy at the University of Heidelberg, whose theory had grown from lack of a satisfying mechanical explanation of growth and regeneration as well as a lack of an explanation for conscious action. In his Gifford Lectures on "The Science and Philosophy of the Organism," delivered at the University of Aberdeen in 1907 and 1908, and later in his *History and Theory of Vitalism*, Driesch suggested the term entelechy to represent the principle that controlled development or regeneration, and the term psychoid for that controlling action. Each appeared to be purposeful in that they made use of matter and of physical and chemical energy to promote purpose. Other terms might just as well have been god, will, providence, or nature. What science knows about death, wrote Driesch, is that "a certain amount of matter that was formerly controlled by entelechy becomes freed from this control, and then obeys the laws of physio-chemical causality exclusively."[107-110]

The debate over the nature and essence of life assumed a major place in literary and scientific discussions in the first decade of the 20th century. Philosophic biologists like J. Arthur Thomson (1861 to 1933) and biologic philosophers such as Henri Louis Bergson (1859 to 1941) turned to explanations that included an extraphysical entity. In his *Creative Evolution* (1911), Bergson attempted to address what he saw as the irregular and unstructured nature of the biologic process. His account of the existence of life was a result of a state of tension between the original creative life force, or elan vital, and the resistance of inert matter from which living bodies must come. For Bergson, the real essence of evolution was in the creative surge of life. Creative evolution was the ceaseless effort of life to reverse the process of matter. "The impetus of life," he wrote, "consists in a need of creation. It cannot create absolutely, because it is confronted with matter, that is to say with the movement that is the inverse of its own. But it seizes upon this matter, which is necessity itself, and strives to introduce into it the largest possible amount of indetermination and liberty."[111]

Later contributors to the philosophy of organism included Alfred North Whitehead, whose *Process and Reality* went beyond Bergson's elan vital by suggesting that nothing in the universe of emergent evolutionism was completely inorganic. Spiritual qualities were a part of matter rather than a force that acted on matter. There was in any period of time an ideal toward which the whole aspired.[112-113]

Despite the renewed vigor that Driesch and others lent to the supporters of vitalistic theory, materialism was not without its adherents. For Hugh Elliot, writing in *Science and Progress in the Twentieth Century* in 1914, vitalism was but the "survival of medieval modes of thought, possessing no greater reality than the cognate problem as to the site of the soul." Although philosophers had formerly attributed almost every natural event to a supernatural or spiritual causation, the perseverance of the inquiring mind now subjected much of what was previously protected within the spiritualistic world to the rigors of science. Despite notable successes, many events remained unrecognizable under existing laws and thus continued to draw on spiritualistic explanations and influences. For the mechanist, this reliance on a spiritual intervention was simply a safety net for those functions of the organism not yet understood within existing laws. Nevertheless, Elliot believed that materialistic explanations would eventually triumph. Each time the vitalist evoked a spiritual or vital force to explain a phenomenon, he was doing little more than asserting a theory that remained beyond the range of human intellect and that recognized the inability to find mechanical forces to provide a full explanation.[73]

Elliot urged scientists and philosophers to dismiss vitalism that not only signified mankind's failure of nerve, but served as a convenient excuse for ambiguity. The crudest reduction of the argument for vitalism was a thinly-disguished sophistry: "Here is a thing I cannot explain mechanically: therefore there can be no mechanical explanation: therefore mechanism is false: therefore vitalism is true."[114-115]

MacDougall's Soul Substance

Within the context of these debates, Duncan MacDougall's experiment might best be understood. From his experiments, MacDougall concluded that any weight loss at death represented the weight of the departed soul. In other words, a "space-occupying body of measurable weight" left the body at death and survived as a "conscious ego" within the earth's ether. MacDougall argued that the substance which left the body at death was not only lighter than the physical body but lighter than the atmosphere as well. Ether was the primary form of all substance—"all other forms of matter are merely differentiations of the ether having varying densities." With the soul substance as a differentiated form of the primary ether, MacDougall concluded that he had at last proven the materialistic conception of the mind, spirit, or soul that continued to exist after the body's death in a quality of separateness distinct from the ether.[1]

MacDougall tested his hypothesis on a man dying of tuberculosis; several hours prior to death, he placed the patient in a bed "arranged on a light framework built upon very delicately balanced platform beam scales." While looking to the man's comfort in his last hours, MacDougall carefully noted a weight loss at the rate of one ounce per hour from respiration and sweating. During this time, he kept adjusting the balance to insure the accuracy of the man's weight. At the moment of expiration, "the beam end dropped with an audible stroke hitting against the lower limiting bar and remaining there with no rebound." MacDougall determined that at that precise moment, the man lost three-fourths of an ounce in weight. Not content with a single example, the physician tested his hypothesis on another dying patient. "In the eighteen minutes that elapsed between the time he ceased breathing until we were certain of death, MacDougall wrote, "there was a weight loss of one and a half ounces and fifty grains." In a third case, he ascertained a loss of one and a half ounces at the moment of death. With each of these tests, MacDougall insisted that there had been no loss from the bowels or kidneys that might account for the weight change. Three additional tests convinced him that

"a substance capable of being weighed does leave the human body at death."[1]

Critics of MacDougall challenged his definition of death and recounted examples of both humans and animals that had died on the operating table only to be resuscitated minutes and even hours later. Ophthalmologist Austin O'Malley, MD, of Philadelphia, for example, thought that MacDougall had confused an "inexplicability" into "a proof that the soul is ponderable" and material.[116] As far as MacDougall was concerned, however, O'Malley had "drunk deep at the springs of learning, but I have a suspicion that he must have kissed the Blarney-stone as well."[2]

Conclusion

Those who sought to bring some form of resolution to the age-old debate believed that the controversy between the vitalists and materialists would end only when each camp recognized the limitations of their respective positions. As long as each considered itself the sole purveyor of truth, agreement would remain impossible. In his presidential address before the zoological section of the British Association for the Advancement of Science, D'Arcy W. Thompson (1860 to 1948) remarked:

> While we keep an open mind on this question of vitalism, or while we lean, as so many of us now do, or even cling with a great yearning, to the belief that something other than the physical forces animates the dust of which we are made, it is rather the business of the philosopher than of the biologist, or of the biologist only when he has served his humble and severe apprenticeship to philosophy, to deal with the ultimate problem. It is the plain bounden duty of the biologist to pursue his course unprejudiced by vitalistic hypotheses, along the road of observation and experiment, according to the accepted discipline of the natural and physical sciences . . . It is an elementary scientific duty, it is a rule that Kant himself laid down, that we should explain, just as far as we possibly can, all that is capable of such explanation, in the light of the properties of matter and of the forms of energy with which we are already acquainted.[117]

Arthur Lovejoy (1873 to 1962), a philosopher from Johns Hopkins University, was similarly displeased with the continued debate. "The term vitalism might, with real advantage to both biology and philosophy," he wrote, "be retired from service," because of the unsettled usage of the term and the lack of a uniform definition.[118] A similar view was expressed by medical historian Fielding H. Garrison (1870 to 1935), who perhaps said it best when he wrote: "Never have medical authors been so verbose and to so little purpose! It is coming to be recognized that vitalism, catalysis, tropisms, and clinical entities are mere verbiage and their ultimate nature unintelligible."[119]

Despite those who tired of the issues, the debate surrounding the Great Biologic Problem continued into the 20th century and represented the intensity of the philosophic mind that resisted the substitution of the how of natural science for the why of metaphysics. Natural science seemed unable to appease the more troubled members who insisted on addressing the issue of first causes. Rather than resolve their differences, scientists and philosophers continued their discussion into the philosophy of organism. The ranks of the combatants, however, were significantly reduced from earlier generations. Curiously, the debate achieved popular status by entering the genre of science fiction. From the ideas of Russian biologist Alexander Oparin in 1936 to the theory of space gods introduced by Erich von Daniken, the catastrophist theory of Immanuel Velikovsky and the interstellar theories of Fred Hoyle and Chandra Wickramsinghe, it appears that reconciliation of the Great Biologic Problem remains somewhere in the future.[120-126]

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Apnea in infancy: pathophysiology, diagnosis, and treatment

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Apnea is the absence of respiratory activity and is a frightening occurrence at any age. Because it has been linked with crib death, or the sudden infant death syndrome (SIDS), in both medical and lay literature, and because it is also a symptom of many life-threatening illnesses in neonates, the evaluation of the infant with apnea has become a major cause for concern for those who provide medical care for infants. The purpose of this report is to review the relevant pathophysiology in the infant under one year of age suspected of having apnea, and to outline the recommended diagnostic and therapeutic approaches to infants presenting with this symptom.

PATHOPHYSIOLOGY

An understanding of the control of breathing is essential in order to treat the infant with apnea. Respiratory activity is intrinsically rhythmic but may be modulated by reflex or voluntarily. The alterations in respiration that take place during hypoxia are examples of autonomic regulation of breathing, while the ability to speak is an example of voluntary control of breathing. Regular respiratory activity has been observed by ultrasound examination in human fetuses as early as 14 weeks of gestation.[1] This activity becomes increasingly regular with increasing gestational age.

Ventilation is regulated to maintain constancy of the levels of oxygen, carbon dioxide, and pH in arterial blood. The ability to maintain adequate ventilation effectively depends on the activity of the striated muscles of respiration, primarily the diaphragm and the intercostals. The activity of these muscles is modulated by the vagal influences involved in the Hering-Breuer reflex that may be of greater significance in infants than in adults due to the unstable chest in newborn infants.[2]

Central generation of respiratory motor impulses is modulated by the peripheral chemoreceptors, the carotid and aortic bodies.[3] The pH of the cerebrospinal fluid also directly influences the activity of the midbrain respiratory centers in the pons.[4] Although hypoxia is initially a respiratory stimulant, this condition may quickly become a respiratory depressant in newborn infants.[5] Other reflexes act to protect the airways from foreign material, and are mediated autonomically via the superior laryngeal nerve.[6]

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The following analysis provides a working basis for the diagnosis and treatment of infants presenting with apnea. For descriptive purposes, three types of apnea may be recognized. Central apnea refers to absence of air movement caused by the lack of a central neurologic stimulus to the respiratory muscles. Apnea following drug overdose is an example of such a cessation of breathing. Obstructive apnea refers to the absence of air movement associated with blockage of the airway. Activity of the respiratory muscles is present in obstructive apnea, but air movement is absent because of the obstruction. If the obstruction is not relieved, and hypoxemia and acidosis become severe, central nervous system depression may ensue. In this manner obstructive apnea may be followed by central apnea. When this occurs, the condition that arises is termed mixed apnea.

CAUSES OF APNEA IN INFANTS

In assessing infantile apnea, the clinician must consider the causes of apnea in infants under one year of age. The diseases associated with apnea are heterogeneous in nature. It is always crucial to bear in mind that apnea may be the manifestation of a serious systemic illness. It is not enough to determine whether or not a patient has apnea and then to administer nonspecific treatment, such as a respiratory stimulant or home apnea monitor. Serious clinical conditions must first be either diagnosed or excluded before nonspecific treatment is initiated. Possible conditions that may be associated with apnea are listed in Table I.

TABLE I. Common Associated Conditions Excluded in the Evaluation of Infants Presenting With Apnea

Infection
Airway obstruction
Gastroesophageal reflux
Metabolic abnormalities
Hypoglycemia
Hyponatremia
Hypocalcemia
Acidosis
Cardiopulmonary disease
Ingestion of drugs or toxins
Seizures
Sudden infant death syndrome (or near-miss)

Prematurity is one of the major causes of apnea in infants.[7,8] Although the cause of this condition is not known, it is probably related to the overall neurologic immaturity of preterm infants, and is most likely central in origin. While significant apnea may be detected as early as the first day of life in small premature infants, apnea of prematurity becomes most troublesome in babies between 5 and 10 days of age. Infants weighing less than 1,500 g at birth appear to be most subject to this condition. Apnea is the most likely cause of the cyanotic attacks in premature infants that were often reported in the medical literature prior to 1965.

Treatment for apnea of prematurity is nonspecific. Some treatment methods include careful monitoring of arterial blood gases; maintenance of a normal arterial pH and P_{O_2}; treatment with respiratory stimulants such as theophylline, aminophylline, or caffeine; and a vigorous effort to rule out other conditions associated with apnea in premature infants. Hypoglycemia, hyponatremia, intracranial hemorrhage, infection (including meningitis), anomalies of the central nervous system, and respiratory distress may be associated with apnea. Apnea in premature infants, if not due to an underlying systemic disease, generally resolves spontaneously when the infant reaches the age of 36 to 38 weeks after conception. Apnea usually does not recur, nor does it require further treatment after resolution. The occurrence of apnea of prematurity does not predict the later occurrence of SIDS.

Infection also appears to be a significant cause of apnea in infants during the first year of life.[9] This is true whether or not the central nervous system is involved. As with many other systemic conditions or diseases associated with central apnea, the exact mechanism by which infection causes apnea is not known. Apnea has been associated with both bacterial and viral infections occurring in the neonatal period as well as with infections occurring later in the first year of life.

Seizures are an important cause of apnea in young infants.[10] Apnea may occur as a result of the cessation of central respiratory activity or as a result of tonic contraction of the respiratory muscles during a seizure. Seizures, like apnea, may be due to many causes. Both seizures and apnea may result from low blood sugar, hyponatremia, asphyxia at birth, or metabolic intoxication (such as aminoacidopathy). Seizures and apnea have also been associated with the presence of central nervous system anomalies and intracranial bleeding. Because of the complexity of the relationship between respiratory regulation and the nervous system, it is apparent that patients with apnea require a thorough evaluation of their neurologic as well as metabolic status.

Airway obstruction has also been associated with apnea.[11] The presence of fluid or solid material in the oropharynx results in a reflex-mediated closure of the glottis. Absence of this reflex activity may result in occlusion of the airway by the foreign material. However, the hyperactivity of this reflex may result in an inability to reverse the closure of the glottis after removal of the obstruction. Failure to overcome reflex closure of the airway may result in central apnea as hypoxia depresses central respiratory activity.

Airway obstruction caused by tonsillar or adenoidal hypertrophy may cause decreased or marginal oxygenation in some patients.[12] These infants may be more prone to central respiratory depression due to hypoxia than infants who do not have airway obstruction. Respiratory depression caused by hypoxia may be a significant cause of apnea during sleep, since respiration is depressed and the chest wall is less stable.[2]

Methods of Study

During the past 25 years apnea has become a much-studied condition. This interest appears to have arisen because of a need to understand apnea of prematurity.[7,8] The advent of methods for continuously recording respiratory activity in small and newborn infants has allowed for the objective observations of breathing. Previously, reports of apnea have referred to color changes in the skin of infants under study known as cyanotic attacks. It was not determined whether heart rate changes were also present; the actual degree of respiratory activity during the cyanotic attack was not noted.[13] The possibility of a discrepancy between the actual respiratory and cardiac activity and the presence or absence of a color change (cyanosis or pallor) has led to many controversies in research, diagnosis, and treatment. For the purposes of this review, apnea will be defined as the absence of respiratory activity noted objectively for a specific period of time. In this report, the definition of apnea does not include changes in heart rate or skin color.

The importance of objective measurement of respiratory activity cannot be overstressed. Physicians and nurses are trained to "average" the respiratory rate over a period of 30 to 60 seconds. In this way they may fail to note periods of apnea that are five to ten seconds in duration. Both medical personnel and laymen are impressed and frightened by significant changes in skin color, such as severe cyanosis or pallor. These color changes may be so startling that the concurrent respiratory activity may not be accurately recorded. Moreover, the apnea that causes the color change may precede the development of cyanosis or pallor. Thus, a pale or cyanotic patient may be observed to have appropriate respiratory activity even though significant apnea may have been present shortly before. In the neonatal intensive care unit, infants may be reported as having bradycardia in the absence of apnea. This may be explained by the fact that apneic attacks of sufficient duration to cause slowing of the heart may not be long enough to trigger the apnea alarm. This phenomenon occurs because apnea alarms tend to average the respiratory rate in the same way that a human observer might, and therefore require a relatively long period of apnea for triggering.

History. The clinical history is the point of entry into the medical care system. An accurate history is particularly crucial in the evaluation of the infant with apnea, since many of the more objective methods of evaluating patients cannot provide answers to the clinical problems presented by the apneic infant. A review of the possible causes of apnea will indicate the specific medical conditions that may be noted: infection, seizures, or gastroesophageal reflux.

In evaluating an infant for apnea the clinician should ascertain how the infant's care-giver determined the in-

fant to be in trouble. The following questions may prove useful in such an evaluation. Did the baby cry? Was the infant awake or asleep? If asleep, what was the baby's position—face up or face down? How long had it been since the infant was last fed? Was the infant warm or cold to the touch? What was the infant's color—pale, blue, or gray? Were any abnormal movements noted, such as jerking or stiffening, or was the infant limp and flaccid? Was the baby breathing? Were any unusual noises heard with the breathing, such as stridor or wheezing? Was the airway clear, or was there food or other material present? What stimulation was necessary to arouse the infant: gentle stimulation (a tough or gentle shake), vigorous stimulation (a hard shake, picking the baby up, etc.), or cardiorespiratory resuscitation (mouth-to-mouth breathing, emergency ambulance corps)?

The purpose of these questions is to obtain information that will aid the clinician in evaluating the patient with apnea. An infant with cyanotic attacks shortly after feeding may have gastroesophageal reflux. Tonic or clonic movements occurring in association with a cyanotic attack may be due to a primary seizure disorder. Wheezing or stridor may suggest disease of the lungs or airways. These symptoms also are useful indicators of the severity and significance of the attack under consideration. The history provided by the parents or care-giver of the infant being evaluated should always be taken seriously. There is no objective laboratory test that will definitely note whether an infant did, in fact, stop breathing. Unless the parents demonstrate overt psychopathology, their history should be taken seriously. It is difficult, however, to make critical judgments regarding mental status when the clinician is confronted with anxious parents who believe that their baby stopped breathing and would not have started again without their help.

In the differential diagnosis of apnea in infancy it is important that the clinician rule out the possibility of aborted crib death or aborted SIDS. At present, SIDS has no known cause and may only be diagnosed with certainty at autopsy. Therefore a negative clinical and laboratory evaluation may indicate either a normal, healthy infant or an infant at high risk for crib death. A careful evaluation of the family and history will aid the clinician in reaching the appropriate conclusion.

Direct observation. The objective investigation of any patient should begin with a physical examination. The patient should always be observed in a warm, comfortable environment. Excessive cold or heat may impose stresses that could cause the patient to hyperventilate and thus obscure the normal resting pattern of breathing. Observation of the patient should include the color of the skin, as well as noting the pattern of any abnormality in perfusion of the skin. Mottling, cyanosis, and the location of these abnormalities of skin perfusion may point to significant circulatory abnormalities as being the cause of sudden color changes. The chest should be observed for rate, depth, and regularity of breathing, as well as for symmetry of respiratory motion. The rhythm of breathing should be noted; apnea or periodic breathing may be present. In order to detect these respiratory irregularities, however, the patient may have to be observed for several minutes. Use of the accessory muscles of breathing should be noted; as with the occurrence of stridor or hoarseness this may indicate an abnormality of the upper airway. The presence of stridor or hoarseness will help localize the abnormality to the area of the larynx. Inspiratory stridor or wheezing often indicates an extrathoracic lesion, while expiratory stridor usually indicates an intrathoracic lesion. This pattern is due to the pressure differential necessary to overcome a breathing obstruction either during inspiration when atmospheric pressure exceeds intrathoracic pressure, or during expiration when intrathoracic pressure must exceed atmospheric pressure. The trachea should be palpated to be sure that it is in the midline and not displaced by a mass that might interfere with breathing. Auscultation of the trachea should be done to localize any obstruction.

Examination of the nose and oropharynx should be done to detect causes of obstruction, such as the presence of polyps or choanal stenosis, cleft palate, or enlarged tonsils and adenoids. Examination of the lungs should include auscultation and percussion in order to detect intrinsic pulmonary disease. The heart should be carefully examined in order to detect any abnormalities of function or rhythm that might be associated with cyanotic spells. Neurologic and developmental evaluations are necessary in order to detect the presence of any abnormalities that might also be associated with cyanotic spells. Thus seizures or a degenerative disease, such as Werdnig-Hoffmann disease, may be the cause of apneic or cyanotic attacks.

Laboratory evaluation. There are no laboratory tests available that can confirm or eliminate the possibility of an apneic attack. In general, the laboratory evaluation of a patient with possible apnea is directed at determining whether or not any diseases capable of causing apnea or cyanosis are present. The acutely-ill infant should undergo studies for infection, including blood culture, spinal tap, and chest radiograph. Biochemical abnormalities such as hypoglycemia, hyponatremia, and hypocalcemia must be ruled out. A blood pH is helpful in determining the presence of a metabolic disease, such as an abnormality of amino acid metabolism, that may result in a cyanotic attack. Abnormalities in arterial pH, P_{CO_2}, and P_{O_2} may also suggest the presence of heart or lung disease. The possible occurrence of seizures or the presence of other neurologic abnormalities may be confirmed by an electroencephalogram (EEG), computed axial tomographic (CAT) scan, or sonogram of the head. For infants who have muscular weakness detected on examination, muscle biopsy and electromyograms may also be indicated.

Apnea has been associated with gastroesophageal reflux. A pH probe is the most definitive means of ruling out this condition. Many infants, especially small, preterm infants, may show gastroesophageal reflux on radiographic examination. The presence of this finding may have little significance in determining the cause of apnea or cyanosis since a barium swallow may reveal gastroesophageal reflux that is not severe enough to cause apnea. However, a barium swallow is helpful in demonstrating the presence of other anomalies of the esophagus or respiratory tract that may be responsible for apnea or abnormalities in swallowing. A barium swallow should be performed in conjunction with a pH probe of the esophagus.

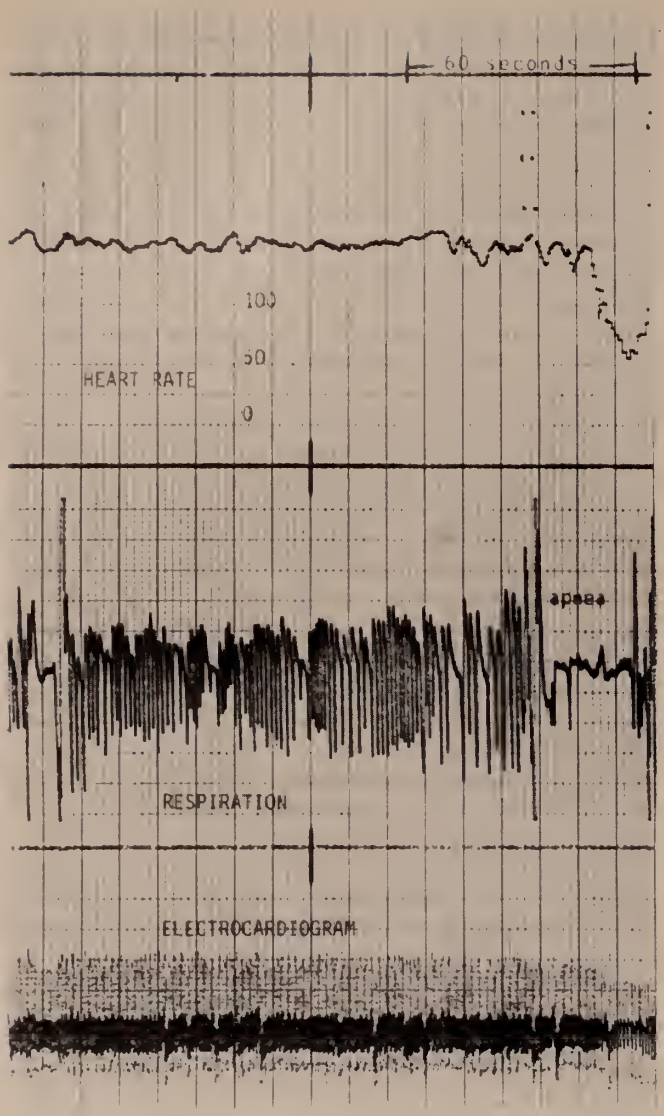

FIGURE 1. Pneumogram demonstrating bradycardia to 50 beats per minute in association with an apneic period at right edge of tracing. A brief period of apnea (approximately five seconds) is seen at the left-hand side of the tracing.

A pneumogram is the fundamental test for detecting the presence of apnea.[13,14] This is a continuous recording of respiratory activity obtained by means of a strain gauge, magnetometer, or impedance pneumogram. These methods rely on detecting motion of the rib cage by electrical or mechanical means. A minimum period of six to eight hours of respiration is necessary in order to adequately evaluate respiratory rhythm in infants. However, these methods have two major defects. The first is that motion of the chest may not represent respiration. Displacement of the recording leads may take place during stretching or seizure activity and may be interpreted as respiratory activity. This technical defect may lead to an underestimation of the amount and duration of apnea. Secondly, respiration can continue in the presence of airway obstruction. Because of the obstruction no air will be exchanged and an attack of cyanosis will occur. However, inspection of a recording of chest wall motion will not reveal that an airway obstruction is present.

As a means of overcoming this technical defect, thermistor beads—temperature sensitive electrical recording probes—or CO_2 probes may be placed in the nostrils of patients undergoing sleep studies. The CO_2 probes are hollow tubes that sense the changes in expired CO_2 taking place during the respiratory cycle. Since these probes are hollow, they are prone to becoming occluded with nasal mucus. Occlusion of a CO_2 probe in the presence of chest wall movement could mistakenly be interpreted as obstructive apnea. The thermistor bead is a potential solution to this problem, and is widely used. However, because of the small tidal volume and rapid respiratory rate of very small infants, the thermistor bead is most useful in older infants and in children (Figs 1 and 2). Apneic spells longer than 15 to 20 seconds or with bradycardia are regarded as abnormal by most observers.

Heart rate is simultaneously recorded along with the respiratory pattern. Slowing of the heart rate during apnea is significant since it indicates the presence of more severe apnea or hypoxemia. The degree of hypoxemia may be more directly estimated if a transcutaneous oxygen monitor or ear oximeter is used. Although transcutaneous monitors for oxygen are frequently used in newborn infants, their use has not been fully validated in older infants. Older infants have thicker skin that causes loss of sensitivity and decreased accuracy in the recording of oxygen levels.

When completed, the pneumogram tracing is inspected for the occurrence of apnea, bradycardia, and hypoxemia. The frequency and duration of apneic spells are noted as is the presence of other unusual respiratory patterns such as periodic breathing. Standards for breathing patterns have been developed for normal infants of various weight and

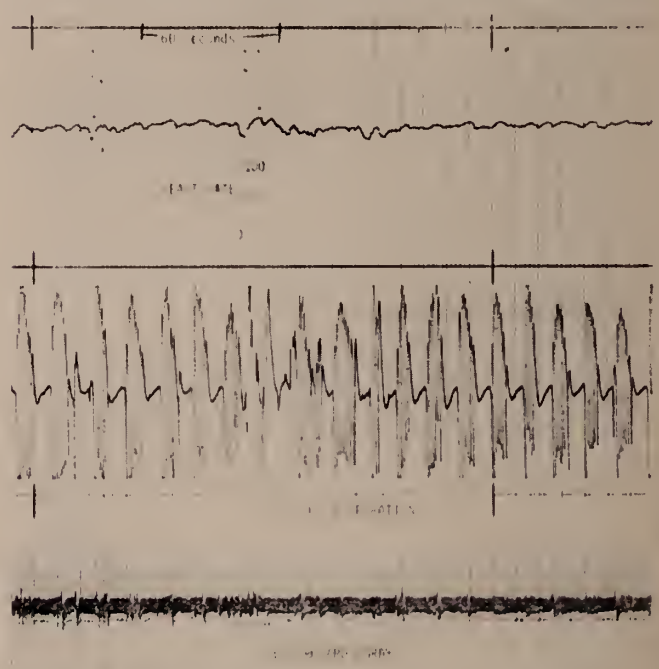

FIGURE 2. Pneumogram demonstrating periodic respiration. Note the lack of bradycardia in association with this pattern of respiration. This pattern differs from Cheyne-Stokes breathing in that Cheyne-Stokes breathing has diminishing amplitude of breathing followed by increasing volume, whereas periodic breathing has abrupt transitions between apnea and respiration.

gestational ages. Preterm infants, siblings of victims of SIDS, and infants resuscitated after a severe apneic attack appear to have increased incidences of apnea and periodic breathing as when compared to normal infants.[14-17] However, there is a significant overlap between the population of normal infants and the "SIDS-at-risk" population. Thus, it may be difficult to predict the risk of SIDS based on a single test, or even on a series of tests. Interpretation of these tests is especially difficult in the asymptomatic newborn infant; results of testing during this period may not predict the development of apnea later.[18,26]

It has been suggested that victims of SIDS may lack sensitivity to carbon dioxide or hypoxemia. Exposure to increased levels of carbon dioxide or reduced levels of oxygen normally results in a stimulation of respiration. Victims of SIDS and their parents and siblings are thought to lack normal sensitivity to these stimuli.[19,20] While this may be true, there is a wide range of variation in response to respiratory stimulation in the normal population, as well as an overlap between the normal population and those at risk. Thus neither of these hypotheses may be used to reliably validate a history of apnea as related by the infant's care-givers, or to consider an infant being evaluated at risk for possible apnea.

As indicated earlier in this article, the causes of apnea in infancy are heterogeneous. The present knowledge regarding the regulation of respiratory activity is as yet insufficient to ascribe a single cause for apnea in infants. Thus the work-up of the apneic patient has an approach that involves the assessment of many systems. Unless the clinical history or physical examination points strongly to a specific cause, the various systems involved in the regulation of respiration must be studied in order to rule out as many causes of apnea as possible (Table II).

Treatment. There are three aspects to be considered in the treatment of apnea in infants. The first aspect consists of the treatment of a specific disease entity, if one is found as a result of the clinical evaluation. The second aspect consists of nonspecific therapy directed toward the stimulation of respiration. The third aspect of treatment consists of monitoring the patient (home monitoring). This method of treatment involves identifying the patient for whom home monitoring is indicated and assisting the family in carrying out this mode of treatment.

TABLE II. Common Indications for Use of Infant Home Cardiorespiratory Monitoring

Indications associated with apnea
Prematurity with persistent apnea and bradycardia
Seizures presenting with apnea
Gastroesophageal reflux
Obstructive sleep apnea
Central apnea
Near-miss episodes (serious, life-threatening)
Indications not associated with apnea
Sibling of victim of SIDS
Infant of drug addict; methadone exposure in utero
Bronchopulmonary dysplasia
Cardiac disease; arrhythmia
Tracheostomy, stridor, airway obstruction
Congenital anomalies
Prematurity

Specific treatment. If apnea is the presenting symptom of an infection, such as group-B beta hemolytic streptococcal septicemia or meningitis, therapy should be directed at combating the infection. This method of treatment would include antibiotics as indicated by bacterial sensitivity testing, appropriate nutrition, and assisted ventilation and circulatory support if indicated. If apnea is found to be the presenting symptom of a seizure disorder, the appropriate therapy would consist of administering anticonvulsants to adequately control the seizures. However, if the seizures prove to be the result of a metabolic disorder, then additional studies of metabolism and appropriate metabolic therapy are warranted. Finally, gastroesophageal reflux presenting with apnea may require thickened feedings, antacids, upright positioning after feedings, and, in selected cases, performance of gastric fundoplication.

These examples indicate how specific therapeutic modalities should be applied when appropriate. In general, this type of therapy is successful for relieving apnea by treating the underlying disorder. Home monitoring, as will be discussed later, is not indicated for all children with apnea. When apnea persists despite appropriate therapy for seizures, for example, or when the family is so anxious that they cannot resume a normal relationship with the child, then home monitoring should be strongly considered.

Nonspecific treatment. Nonspecific treatment of apnea consists of the use of various respiratory stimulants. Most clinical experience with pharmacologic respiratory stimulants—caffeine, theophylline, doxapram, almitrane, naloxone, or estrogens—has been obtained in preterm infants, in patients with drug overdose or metabolic intoxication, and in adults. There is relatively little published data on the pharmacologic treatment of apnea in children between the neonatal period and one year of age.

In preterm infants, therapy with methylxanthines, such as caffeine, aminophylline, or theophylline, is generally successful.[21,22] These drugs appear to act as respiratory and metabolic stimulants. Increased sensitivity to CO_2 has been demonstrated after the administration of theophylline.[23] This finding does not completely explain the mechanism of action of these drugs since increased sensitivity to CO_2 cannot be demonstrated in preterm infants receiving low doses of theophylline who also demonstrate a reduction in apnea of 60 to 80% of pretreatment levels.[22] Methylxanthines have significant metabolic and neurologic effects in preterm infants. Following treatment with theophylline, preterm infants have increased amounts of active sleep and an increased metabolic rate.[24,25]

Methylxanthines have been prescribed for the relief of persistent apnea of prematurity, and have been given to premature infants after discharge from the neonatal intensive care unit. Treatment of persistent apnea after discharge from the neonatal unit has the advantage of shortening the hospital stay of preterm infants. Such treatment following discharge from the hospital requires assurance that no other cause of apnea is present. Preterm infants may have airway obstruction as a result of prolonged endotracheal intubation, and they also are more likely to have gastroesophageal reflux than full-term infants. Central nervous system lesions, such as the residual

of neonatal infections or the result of intracranial bleeding, may also cause persistent apnea in preterm infants. The clinician must conduct a vigorous search for these causes before prescribing medication for symptomatic relief and discharging the infant from the hospital.

Apnea of prematurity is the most common form of apnea seen in early infancy. Infants, especially those that are preterm, presenting with apnea following discharge from the nursery should not be automatically considered candidates for treatment with methylxanthine. While apnea of prematurity may respond to methylxanthine drugs, other forms of apnea may not respond. This is especially true of infants whose apnea may represent an aborted SIDS occurrence. Although some research centers have gained experience with respiratory stimulants such as almitrane, doxapram, and naloxone in older infants, their general use cannot be recommended at present.[27] It cannot be too strongly emphasized that at present most clinical experience with nonspecific pharmacologic treatment of infants with apnea is based on the treatment of apnea of prematurity. With increasing knowledge the appropriate use of respiratory stimulants for the treament of older infants with central apnea will be determined.

At present, it appears that the major effect of the methylxanthines is to provide stimulation to the central nervous system so that regular respiration is restored in preterm infants. Physical stimulation has been provided in neonatal intensive care units by means of swing hammocks and oscillating water beds.[28] Gentle stimulation may also be provided at the bedside by nurses or clinicians responding to a heart rate (bradycardia) alarm or apnea alarm. If cyanotic attacks are neither frequent nor severe, pharmacologic therapy for apnea need not be instituted.

The rate of occurrence of cyanotic attacks for which drug therapy becomes appropriate is a matter of individual clinical judgement based on careful evaluation of the patient. Since abnormalities such as sepsis, meningitis, intracranial bleeding, and hypoglycemia may also occur frequently in preterm infants, they should receive careful consideration when treatment for apnea of prematurity is instituted. Symptomatic therapy with drugs such as methylxanthines should not be undertaken unless a thorough diagnostic evaluation has been initiated. This diagnostic evaluation should be based on a careful review of the history and physical examination, and should be comprehensive enough to evaluate the patient for all of the treatable causes of apnea.

Symptomatic treatment and home monitoring may follow only after completion of the evaluation. For the infant with an acute presentation of apnea, this evaluation should include appropriate cultures to rule out systemic infection and an evaluation of blood chemistries to detect such abnormalities as hypoglycemia or acidosis. A chest radiograph not only is part of the evaluation for infection but also enables the clinician to evaluate the patient for the presence of cardiac or pulmonary disease. If seizures are suspected—either because of the clinical description of the apneic attack or because of an abnormal neurologic examination—an EEG and head sonogram or CAT scan would be appropriate. If the episodes of apnea occur in conjunction with feeding, an esophageal pH probe to detect the presence of significant gastroesophageal reflux is indicated.

Due to the wide variety of clinical presentations and possible causes of apnea in infants, a genetic evaluation for all patients with this symptom cannot be described. It is the clinician's responsibility to evaluate the patient, determine the differential diagnosis, and assign appropriate priorities to the various diagnostic entities as indicated by this initial assessment. Every patient need not be evaluated for each cause of apnea.

Home monitoring. Because of the association between apnea and the occurrence of SIDS, home monitoring has become widely recommended as a means of protecting the infant who presents with apnea. Recent studies indicate that approximately 15% of infants who succumb to SIDS develop symptoms of apnea or of another respiratory abnormality before death.[29] Although little may be done for the 80 to 85% of infants who die without showing antecedent symptoms, it may be possible to help the 15% of symptomatic infants if they are recognized and treated. Initial reports indicate a mortality rate as high as 40% for infants presenting with apnea.[15] This initial group of infants was highly selected, and consisted of infants now recognized to be at very high risk for SIDS. Subsequent experience has indicated a progressively lower death rate among monitored infants.[30] Mortality in home monitor programs is now so low that many clinicians have been led to question the relation between apnea and SIDS (Fig 3). With the mortality rate approaching zero in many large series of infants, it may be that apnea in older infants is not an early symptom of SIDS but may represent a different disorder. This is a special problem for the clinician faced with a child whose physical and laboratory examinations are within normal limits, but whose parents present a convincing story for their baby having had an apneic spell at home.

It is this inability to objectively evaluate parents' histo-

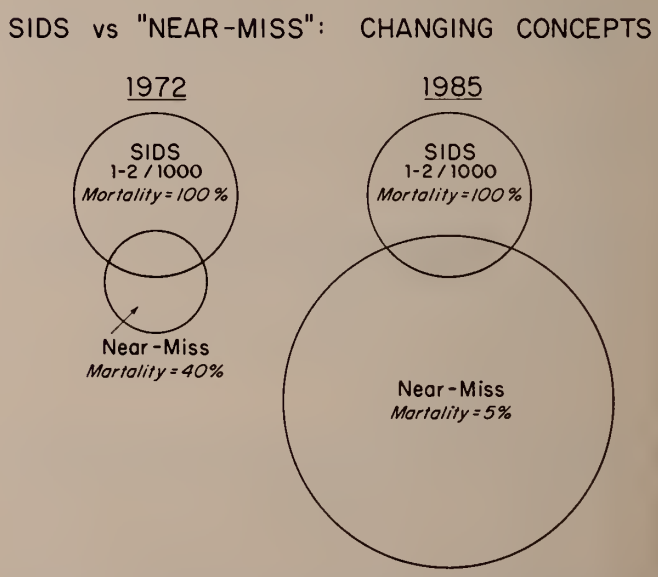

FIGURE 3. This diagram depicts the changing concept of SIDS versus "near-miss" SIDS. In 1972 it appeared that "near-miss" SIDS had a relatively high mortality rate, being 40%.[15] With increased concern, it now appears that "near-miss" infants have an overall mortality of 5% or less.[30] This compares with a mortality rate of 100% in victims of SIDS, approximately 15% of whom have symptoms prior to death.[29]

ries that probably leads to the wide discrepancy in the rates with which apnea monitors are prescribed for use at home. During 1983 statistics collected by the New York State Department of Health revealed that apnea centers varied from 15% to 75% in the rate with which they prescribed home monitors to infants evaluated for apnea.[31] Monitors were prescribed for a wide variety of conditions including seizures, prematurity, and gastroesophageal reflux, as well as for apnea. In part, this wide range in the rate of prescription of home monitors must be due to the poor ability of any test to predict the later occurrence of SIDS, particularly when the tests are performed during the neonatal period.

The incidence of SIDS is 1 to 2 per 1,000 infants in New York State, if unselected births are considered.[30,31] High risk groups, such as siblings of SIDS victims and preterm infants, have a risk for SIDS five to ten times that of the general population. These data suggest that even in the high-risk groups, more than 99% of children will never develop SIDS. It should be realized that approximately 5% of the infant population today were once in premature nurseries or neonatal intensive care units. Considering this large population of potentially high-risk patients, the high cost of home monitoring should be taken into account. Is it medically justified to prescribe a monitor for home use that costs approximately $250 to $300 per month for an infant simply because that infant is a preterm infant but lacks any other indication for apnea monitoring?

Home apnea monitors should be used only in specific situations. The first and primary indication for monitor use is that of an infant who has medically-documented apnea, either because resuscitation was required (such as with cardiorespiratory arrest) or because significant apnea has been documented on a pneumogram. The apnea may be either the result of another illness, such as epilepsy, or may be primary, central apnea. A second situation where home monitoring is indicated is in the subsequent sibling of a victim of SIDS. While not all families who have lost an infant because of SIDS request a monitor for later children, many families are so traumatized by their previous loss that they require the assurance of a home apnea/heart rate monitor. A third situation where a home monitor may be considered is when a preterm infant has persistent apnea but has reached a weight and maturity compatible with discharge to the home.

Infants discharged from a neonatal intensive care unit, including infants of drug addicted mothers, form a high risk group for sudden infant death. However, the laboratory and clinical evaluations presented do not permit selection of the 0.5 to 1% of preterm infants who may develop SIDS. Thus a home monitor should be prescribed only if apnea and bradycardia prevent the discharge from the unit of an otherwise healthy preterm infant.

A fourth situation that warrants home monitoring is in the infant with an abnormality such as cardiac arrhythmia or tracheostomy. If apnea is not a problem for these patients then a heart rate monitor is sufficient. The clinical problem presented by these infants is that of a heart rate abnormality following the development of an arrhythmia or due to an obstruction of the tracheostomy.

With the exception of the infant of the family that had lost a child previously to SIDS, all of the categories of infants mentioned earlier require a thorough diagnostic evaluation before a monitor may be prescribed in order to eliminate the possibility of other serious systemic disorders requiring treatment. However, a diagnostic evaluation may not be required for asymptomatic siblings of victims of SIDS whose parents desire a home monitor. A normal pneumogram does not necessarily reassure the clinician that an infant is normal (although a normal pneumogram is usually reassuring to the family), or that a pneumogram is highly predictive of an abnormality.[18] For such families, a home monitor may be prescribed for the new infant without an extensive laboratory evaluation.

Infants discharged from the hospital on monitors require periodic evaluations with a complete history and physical examination as part of their continuing care. The home monitor may be discontinued if there have been no alarms requiring resuscitation of vigorous stimulation in the preceding two to four month period, and if the anniversary of the loss (age at time of death) of a previous victim of SIDS has passed. Many families of victims of SIDS see this anniversary as a critical obstacle that must be safely passed. Once this age has been reached, the family gains confidence about the new infant and becomes ready to consider the discontinuation of the home monitor. Although some clinicians require normal pneumograms before discontinuation of a home monitor, it should be stressed that the prognostic value of these tests is not high. More reliance may be placed on a history of prolonged home monitoring without significant apnea or bradycardia alarms.

Parents must be prepared to discontinue a home apnea monitor. Many parents come to rely on the monitor; it offers them security and comfort. Although the infant has fulfilled the medical criteria listed above for discontinuation of monitoring it does not necessarily mean that the parents are ready to remove the monitor. The presence of the appropriate clinical criteria may be used to reassure parents that their infant is doing well, and that they may discontinue the monitor when they feel they are ready to do so.

Evaluation of the family is crucial to the success of home monitoring. Parents must understand that infants have died even while on home monitors. The monitor will alert the parents to the possibility that a serious, life-threatening event may be taking place. Although a home monitor can signal the occurrence of cardiorespiratory arrest, the parents must be made aware that they will not necessarily be able to reverse the event. They must then take the responsibility for resuscitation of their infant. The parents become "first responders" in the event of a cardiorespiratory arrest and therefore must be competent in cardiopulmonary resuscitation. If a family cannot cope with these two possible situations, then they cannot be considered for home monitoring.

A complete social service and nursing evaluation of each family should be undertaken before home monitoring is offered. Compliance on the part of the family cannot be taken for granted by the prescribing physician. Support of the monitor by a competent vendor—including 24-hour, 7-day availability for service in the home and adequate instruction of the parents—is crucial to insure its

efficient operation. Local telephone and electric companies must be contacted since families with infants on apnea monitors are critically dependent on their monitors to be in operation at all times. These families must also be able to maintain emergency communication with their health care team.

Summary

Apnea in infants is a symptom that has been associated with many diseases and conditions although it is perhaps best known for its association with SIDS. This condition has been comprehensively reviewed in the literature,[30-32] providing timely information on the status of apparatus for detection, recommended treatment, and ongoing research on this problem.

It is important to realize that although research has so far failed to reveal the cause of SIDS, this research has revealed other associations between apnea and disease in infants. The physician confronted with an infant with a history of apnea must be prepared to evaluate the baby for the possible presence of these conditions and to prescribe appropriate therapy when available. A comprehensive approach to the infant with apnea will be more likely to yield a satisfactory clinical result, and will provide the best outcome for both the infant and family.

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Liver lesion with fever and abdominal pain

Case History

Deepak Bramhavar, MD (Fellow, Department of Radiology): A 70-year-old woman came to the emergency room of the State University of New York Upstate Medical Center after three days of high fever, profuse perspiration, and diarrhea. On the evening of admission she developed crampy lower abdominal pain associated with spiking fever and chills. Her significant past medical history included hypertension and a cholecystectomy with a choledochoduodenostomy three years earlier. Physical examination revealed a slightly tachypneic obese woman with a temperature of 40°C. Auscultation revealed a grade II/VI ejection systolic murmur and bibasilar rales. No abdominal masses were felt. Routine laboratory data included normal serum electrolytes, a hematocrit of 30.8%, and a white blood cell count of 18,000/μL. Liver function studies revealed an alkaline phosphatase of 397 IU; lactate dehydrogenase, 326 IU; serum glutamic oxaloacetic transaminase (also known as aspartate aminotransferase), 113 IU; and total bilirubin, 1.3 mg%. A chest radiograph, abdominal sonogram and computed tomography (CT), and nuclear imaging studies of the liver were performed.

FIGURE 1. Technetium 99^m liver-spleen scan demonstrating photopenic area in the inferior aspect of the right lobe (arrows). Three views, left to right: AP, RAO, right lateral.

Radiologic Discussion

Michael E. Berlow, MD (Assistant Professor, Department of Radiology): A radionuclide liver-spleen scan with Tc^{99m} sulfur colloid (Fig 1) revealed a well-defined photopenic defect in the inferolateral aspect of the right lobe of the liver. The differential diagnosis of this space-occupying lesion in the liver includes a cyst, hematoma, abscess, and a benign or malignant neoplastic mass. Considering the patient's acute symptoms, an abscess should be strongly considered.

A sonogram of the liver performed several hours after the liver-spleen scan (Fig 2) demonstrates a corresponding abnormality in the right lobe of the liver. The lesion is hypoechoic in texture; the appearance is not characteristic of a cyst and is atypical of a hematoma. However, an abscess or neoplasm could have such an appearance.

An In^{111}-tropolone-labelled white blood cell study (Fig 3) reveals intense leukocyte accumulation in the same area of the right lobe of the liver. This result is specific for an abscess.

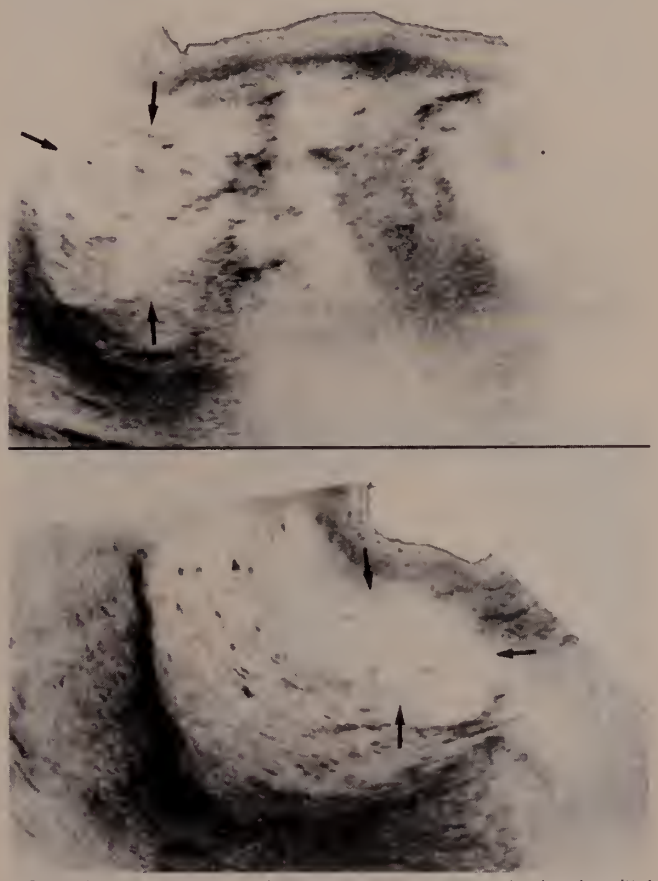

FIGURE 2. Right upper quadrant sonogram, transverse (top) and sagittal (bottom) images. A predominantly hypoechoic area in the parenchyma of the right hepatic lobe is consistent with a space occupying lesion other than a cyst (arrows).

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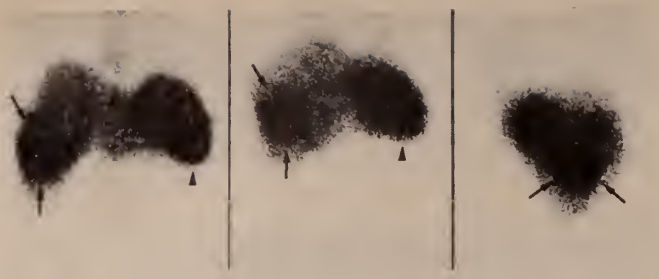

FIGURE 3. Labelled white blood cell study: AP, RAO, right lateral views from left to right. Intense accumulation of radioactivity in corresponding area of right hepatic lobe (arrows). Normal background activity is present in surrounding liver. Normal intense activity in left upper quadrant (arrowheads) is in spleen.

The CT scan was performed before surgery for a more precise anatomic definition of the location and extent of the abnormality. A corresponding poorly-marginated area of diminished attenuation was identified (Figs 4,5). In 30% of abscesses, gas may be identified in such a lesion on CT scan. The lesion noted here lacks such specificity and could also represent a neoplastic process.

Dr Bramhavar: An exploratory laparotomy was performed with drainage of purulent material from the hepatic lesion. A stenosis at the site of the choledochoduodenostomy was identified and this anastomosis was revised. The aspirate from the abscess was sent for laboratory examination.

Clinical Diagnosis

Hepatic abscess, most likely related to partial obstruction of the choledochoduodenostomy.

Pathologic Discussion

Bedros Markarian, MD (Associate Professor, Department of Pathology): Material from the liver abscess was submitted for microbiologic examination; culture yielded *Escherichia coli* sensitive to cephalosporins. Liver abscesses generally affect patients over 40 years of age and are most commonly associated with obstruction and subsequent infection of the biliary tree.

When an organism is found, two thirds are due to *E. coli*, as in the case reported here; *Streptococcus faecalis* and *Proteus vulgaris* are also found. This case is quite typical with elements of obstruction of the common bile duct and the isolation of *E. coli* organisms.

FIGURE 4. CT scan without intravenous contrast. A subtle area of decreased attentuation is present in the right lobe of the liver (arrows). Air is present in bile ducts (arrowheads) consistent with a choledochoduodenostomy.

Discussion

Dr Bramhavar: The localization of a septic focus in a febrile patient is often a difficult clinical problem. A variety of noninvasive radiologic and nuclear medicine studies are performed for the evaluation of such patients. Since plain abdominal radiographs are often nonspecific, other imaging techniques such as ultrasound, CT scans, and nuclear studies are important for identifying the site of the infection.

Among the noninvasive imaging modalities available, ultrasound generally takes the least amount of time and is the least expensive study. The improved resolution of real time sector scanning has increased diagnostic accuracy up to 92% in the detection and localization of focal hepatic lesions.[1] The typical ultrasound appearance of a liver abscess is a predominantly sonolucent lesion with ill-defined margins associated with varying degrees of internal echoes depending on the stage of abscess evolution. The internal echoes are caused by aggregates of purulent material or necrotic tissue. Although ultrasound is sensitive and is an excellent screening procedure for focal liver lesions, it lacks specificity. An abscess is often indistinguishable from a necrotic tumor, infected hematoma, or complicated cyst. A specific diagnosis, however, is often established by ultrasound-guided needle aspiration. Ultrasonic examination is limited by marked obesity, by the presence of overlying bowel gas, and by overlying bony structures such as ribs. Transducer-skin contact is necessary for ultrasound examination, and therefore this study may not be feasible in postoperative patients.

Abdominal computed tomography is the most sensitive examination for the identification of focal hepatic lesions. A sensitivity of 96% in the detection of focal liver lesions has been reported.[2] A liver abscess is visualized as an area of low attenuation within the liver. The density measurements obtained are usually between that of normal liver parenchyma and water. Demonstration of a well-defined rim of enhancement after the administration of intrave-

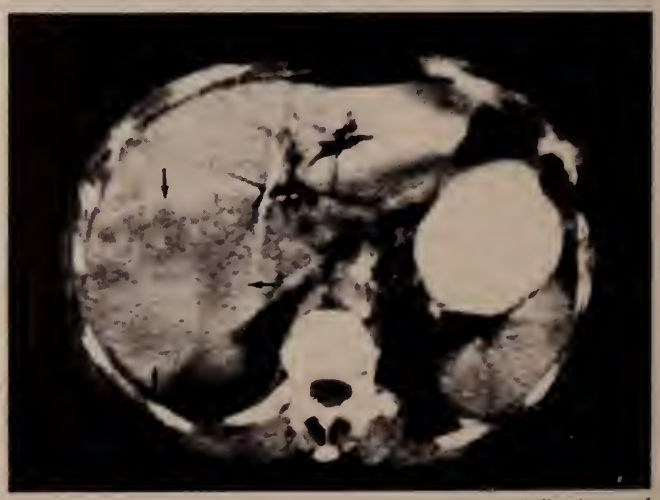

FIGURE 5. CT scan after intravenous contrast. A better defined area of diminished attenuation is identified (arrows).

nous contrast corresponding to the abscess wall supports the diagnosis of a liver abscess. As with ultrasound, the differentiation of a liver abscess from a necrotic tumor and complicated cyst may not be always feasible even after contrast enhancement. However, identification of gas —present in about 30% of all cases—on CT scan is specific for an abscess.

Many radionuclide liver imaging techniques have been used in the evaluation of liver lesions. Lesions larger than 1 cm in diameter are detected on routine sulfur colloid liver-spleen scans. Liver scintigraphy is an excellent screening procedure but lacks specificity.

In the diagnostic work-up of a febrile patient, Gallium^{67} citrate has been used for the detection of a liver abscess. However, gallium abscess imaging has several limitations. An abnormal study is often nonspecific since hepatic neoplasms and other disease processes are associated with focal areas of gallium concentration. Since the time required for gallium accumulation in abnormal tissue is long (up to three days), its role in the evaluation of an abscess in critically ill patients is limited.

Various indium compounds (In^{111}) have been used for tagging autologous white blood cells. At the institution reported here indium labelled tropolone is used. Some researchers have reported a 15-fold increase in the concentration of indium-labelled white blood cells in an abscess as compared to gallium concentration at the same site.[3] A diagnostic accuracy of 98% has been reported for the localization of a site of infection[1] in this manner. In the liver, small abscesses may be obscured by normal background radioactivity. However, larger abscesses such as in this case are accurately detected by this study. Like other imaging modalities, this technique has limitations. Since the accumulation of labelled white cells depends on the ability to concentrate leukocytes in an abscess, patients with leukopenia are likely to give a false negative result.[4] Similarly patients on steroid therapy, hemodialysis, hyperalimentation, and those with hyperglycemia may give poor results due to altered leukocyte function. False negative studies have also been reported with previous antibiotic therapy. Chronic thick walled abscesses may lack enough inflammatory reaction to be detected.[2]

The selection of the primary imaging study in the detection of a liver abscess should be influenced by the clinical presentation. At this institution, patients who are acutely ill and strongly considered to have a hepatic abscess are initially evaluated by CT scan or ultrasound. Percutaneous aspiration and drainage of abnormal collections under the guidance of either method is then available. Negative studies in this group of patients, or in less critical patients in whom the suspicion of an abscess is lower, are examined with a labelled leukocyte study.

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Acute posttraumatic hypertension in fibromuscular dysplasia of the renal artery

Subintimal hemorrhage treated by percutaneous transluminal angioplasty

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Blunt trauma is an uncommon but well-recognized cause of renal artery injury. The majority of these injuries result in renal artery thrombosis.[1,2] The following case is unusual in that minor trauma resulted in subintimal hemorrhage in a vessel already affected by fibromuscular dysplasia. The lesion was diagnosed on arteriographic examination and successfully treated by percutaneous transluminal balloon angioplasty (PTA).

CASE REPORT

A 23-year-old woman fell at a railroad station and sustained a blunt injury to the right flank. The patient landed prone, and a suitcase strapped over her shoulder struck her right flank. Within two days, the patient developed signs of acute hypertensive encephalopathy: headaches, tinnitus, nausea, and vomiting. She was seen at a local emergency room and her blood pressure was noted to be 190/150 mm Hg. Although the woman had had no previous abnormal blood pressure levels, she was discharged to the care of her private physician. Her symptoms worsened and on the following day she was admitted to the same hospital, where her blood pressure was recorded at 210/180 mm Hg.

The initial radiographic evaluation included ^{131}I-hippuran and 99m Tc-glucoheptonate renal scans, a rapid sequence intravenous urogram, and a computed tomographic (CT) scan of the abdomen with contrast. The radionuclide studies demonstrated a slight but definite decrease in right renal perfusion. The intravenous pyelogram was interpreted as normal. The CT scan demonstrated a dense right nephrogram on delayed images consistent with decreased perfusion and delayed excretion. The patient was placed on antihypertensive medication sufficient to maintain her blood pressure at 150/90 mm Hg and transferred to Lenox Hill Hospital for further evaluation.

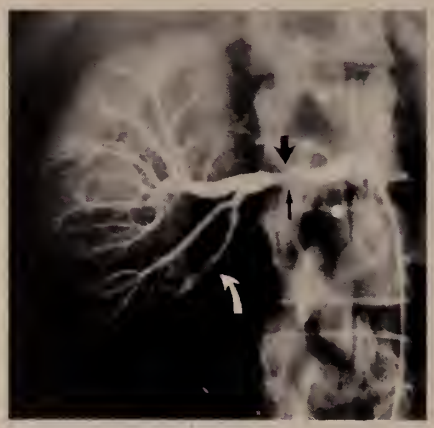

FIGURE 1. Lobulated contour of superior aspect of main right renal artery consistent with fibromuscular dysplasia (large arrowhead) and smooth indentation of inferior border due to subintimal hemorrhage (straight arrow). Narrowing of inferior pole branch artery was transient and due to spasm (curved arrow).

On admission to this hospital, the patient's blood pressure was 150/90 mm Hg and the symptoms of acute hypertensive encephalopathy had abated. Chest radiograph and routine laboratory data were normal. Peripheral renins were markedly elevated at 70.5 mg/mL/h (normal, 1–5 mg/mL/h). Selective renal vein catheterization was attempted but was unsuccessful due to unusually tortuous iliac veins. A Tc-GHA renal scan showed decreased perfusion and delayed excretion by the right kidney. Abdominal aortography and selective right renal arteriography demonstrated evidence of subintimal hemorrhage in the mid-right renal artery and features of fibromuscular dysplasia (Fig 1).

A vascular surgical consultant advised a conservative course due to the high risk of further intraoperative damage to the renal artery. The patient was discharged from the hospital on propranolol hydrochloride, 240 mg two times a day, and hydralazine, 75 mg two times a day, to be followed in a clinic setting and perhaps to be considered as a candidate for PTA at a future date. Six weeks later a repeat Tc-GHA renal scan showed marked improvement in renal perfusion and excretion although the patient remained hypertensive.

Two months later—four months after the initial injury—PTA of the right renal artery was performed with immediate normalization of the patient's blood pressure (Fig 2). The patient did well for three months, but symptomatic hypertension subsequently recurred. Repeat angiography disclosed stenosis of the main right artery beginning at the distal end of the previously treated segment and terminating just proximal to the bifurcation. PTA was again performed with immediate normalization of the blood pressure (Fig 3). The patient has remained asymptomatic and normotensive for one year following the second procedure. A recent 99m Tc-DPTA renal scan demonstrated symmetric perfusion of both kidneys.

DISCUSSION

Blunt trauma infrequently injures normal renal arteries. Ross and colleagues[3] evaluated 176 patients who had sustained blunt trauma to the flank or abdomen and identified only four with a renal artery injury. The most common injury is unilateral thrombosis

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FIGURE 2. Predilatation arteriogram shows decrease in size of subintimal hemorrhage and persistence of features of fibromuscular dysplasia (left); postdilatation arteriogram shows successful restoration of normal luminal caliber (right).

that accounts for almost one half of the reported cases.[1,2] Intimal tears with dissection but without thrombosis are much less common; stenosis is even less common and accounted for only five of 188 cases of unilateral injury described in one review.[1] Unrecognized vessel wall injury after trauma with subsequent fibrosis has been implicated as a cause of renal artery stenosis and renovascular hypertension.[3]

Several mechanisms have been proposed to account for these injuries. The most prevalent theory originally proposed by Collins and Jacobs[2] in 1961 implicates the rapid movement of a kidney with respect to the aorta. This movement results in the stretching of the renal artery with a resultant intimal tear. Luminal blood may then dissect under the intimal flap and platelet aggregation at the site of the injury may result in thrombosis. Severe stretch injuries may also lead to avulsion of the renal artery. According to McAninch,[4] this theory explains the increased frequency of left renal artery injuries resulting from the relative hypermobility of the left kidney as compared to the right.

Compression of the right renal artery against the spine may contribute to some of the less common right renal artery injuries.[5] Lohse and associates[6] describe a variant of Collins' theory by postulating that a direct blow to the back causes each kidney to move posterolaterally, thus pulling against each other at their point of fixation at the aorta. Ross and coworkers[3] describe posttraumatic subintimal hematomas and attribute them to either extravasation of the intraluminal blood through an intimal tear, or subintimal hemorrhage due to injury of the vasa vasorum in the tunica media of the arterial wall.

Hypertension following renal trauma is variable in its incidence, time of onset, and course.[7] In a review of 93 patients, 31 (30%) with unilateral injury who survived without immediate nephrectomy developed hypertension.[1] In another study 23 of 40 patients (57%) with renal artery injuries became hypertensive.[8] The onset of hypertension after trauma varies from immediately after the event,[9-12] to as late as four years afterwards.[7] This variance in time of onset may reflect differences in renal ischemia, sodium intake, and contralateral function as well as genetic factors. The outcome of posttraumatic hypertension is also variable. Several authors have reported spontaneous resolution of posttraumatic renovascular hypertension.[7,11,12] Resolution has also been reported after late revascularization or nephrectomy.[1,7,8]

In the case reported on here, blunt trauma was superimposed on fibromuscular dysplasia which in itself is a well-recognized source of occlusive lesions of the renal arteries. DeBakey reported that 13% of such occlusive lesions were due to fibromuscular dysplasia.[13] Spontaneous dissection occurs in about 5 to 10% of cases of fibromuscular dysplasia[14] thus accounting for a large percentage of all cases of spontaneous dissection of a renal artery.[12] This propensity toward spontaneous dissection suggests that the vessel wall may be weakened by the underlying disease. Thus, even minor trauma may cause dissection or subintimal hemorrhage in a diseased artery. Such an event was seen in this patient, who developed a subintimal hematoma following relatively minor trauma. A similar case of trauma superimposed on fibromuscular dysplasia in the carotid artery was described by Young and colleagues.[15] Since the carotid artery was involved in that case, immediate surgical intervention was necessary. However, repeated mild and unrecognized vascular injury was considered a factor in both the pathogenesis of fibromuscular dysplasia and the occlusive lesions frequently seen associated with it.

Recognition of the patient with a renal artery injury resulting from blunt trauma may be difficult. Careful examination is necessary as even minor trauma may result in an arterial injury. The patient may have hypertension as a presenting symptom but more likely will present with other evidence of renal or abdominal trauma. Epigastric or flank pain is usually present, as is proteinuria.[5,9] Hematuria is often noted but is not a reliable sign.[1,9,16] Intravenous urography demonstrates unilaterally absent or decreased function.[1,9,16] Arteriography, however, is almost always diagnostic.[1]

The ability to detect trauma to the

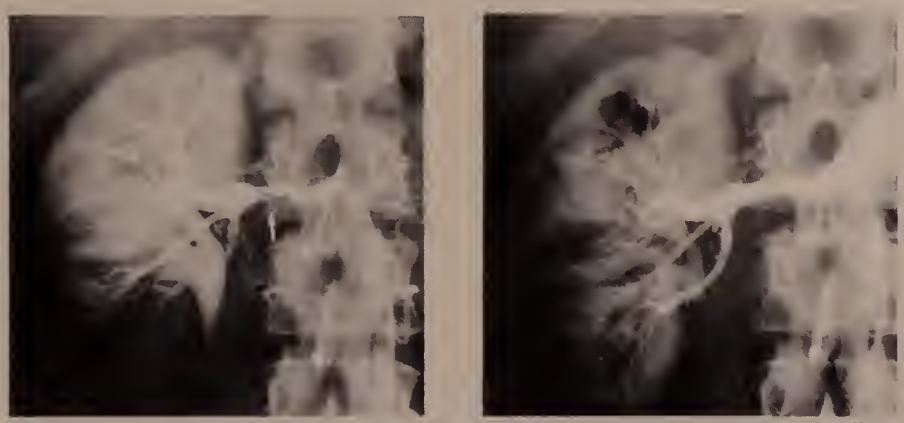

FIGURE 3. Arteriogram demonstrates stenosis distal to previously dilated area extending to bifurcation (left); postdilatation arteriogram shows restoration of normal luminal caliber (right).

arterial wall on arteriography depends on the degree of involvement of the wall and the evolution of the process. If disruption of all three layers of the arterial wall occurs, a pseudoaneurysm may form and may be visualized as extravasation of contrast into an encapsulated area associated with the arterial lumen. A tear involving only the initimal layer usually leads to platelet aggregation and thrombosis of the vessel. On arteriography this is visualized as a sharply marginated occlusion of the artery. Less frequently, contrast may dissect under the torn intima and produce an intimal flap seen as a linear lucency within the contrast-filled artery. Occasionally, as seen in this case, a hematoma may develop within the wall itself if none of the layers are actually disrupted. Such a hematoma has the appearance typical of intramural extraluminal lesions and is characterized by a smoothly marginated, eccentric defect with obtuse angles. The rapid decrease in the size of this defect further supports the diagnosis of a subintimal hematoma.

The few reports of damaged but patent renal arteries following blunt trauma do not provide sufficient data to develop conclusive recommendations regarding management. Furthermore, variations in clinical status and the degree of renal ischemia necessitate that each case be treated individually. However, because surgical attempts at revascularization often yield poor results and frequently necessitate nephrectomy,[1,4,9,16] an initially conservative approach is advisable if the kidney is tolerating its ischemic state. Such an approach is supported by previous observations that posttraumatic hypertension may resolve spontaneously[7,11,12] and even nonfunctioning kidneys may spontaneously regain function.[3,12] If at a later time definitive treatment becomes necessary, surgical revascularization or PTA may be attempted. This latter technique, that is widely used to treat the presumably nontraumatic renal artery stenoses of fibromuscular dysplasia, was used successfully in this case to treat a posttraumatic stenosis superimposed on FMD. However, the rapid recurrence of stenosis following the initial dilatation suggests that the acute injury had not completely healed, and that the dilatation itself may have been a causative factor in producing the more distal stenosis. Thus if immediate surgical repair of a partially occluded artery is not performed, PTA perhaps should be delayed until sufficient time has elapsed to allow for complete healing. Such a delay may reduce the possibility of causing irreparable damage to an acutely injured vessel and recurrence of the stenosis.

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Endocarditis due to *Corynebacterium pseudodiphtheriticum*

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Diphtheroids (*Corynebacterium* species) are a rare cause of bacterial endocarditis. Approximately 100 cases of endocarditis caused by diphtheroids have been reported in the literature since 1893; most were associated with cardiac surgery, prosthetic valves, or deformed natural valves. Diphtheroids cause less than 0.3% of cases of endocarditis in general and are responsible for approximately 2% of cases of endocarditis in intravenous drug abusers.[1,2]

Nine cases of endocarditis caused by *Corynebacterium pseudodiphtheriticum* (also known as *C. hofmannii*) have been documented.[2–9] Three of these cases occurred concurrently with endocarditis due to other organisms, and three cases occurred in prosthetic valves. The following is a report of the successful treatment of a 71-year-old man with *C. pseudodiphtheriticum* endocarditis of a native mitral valve.

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Case Report

A 71-year-old man was admitted to a local hospital with a one-week history of fever, anorexia, diaphoresis, bilateral pedal edema, generalized weakness, and lethargy. Past medical history revealed a murmur of mitral regurgitation for more than 20 years. The patient denied any intravenous drug abuse or recent dental work. Three sets of blood cultures drawn on admission were negative and an echocardiogram revealed no cardiac vegetations.

The patient was referred to Erie County Medical Center on the fourth day following his initial hospital admission. Physical examination revealed a fever of 102° F, jugular venous distention, coarse bibasilar rales on lung examination, a grade III/VI holosystolic murmur, and pitting edema of the lower extremities. There were no Roth spots, Janeway lesions, Osler nodes, or splinter hemorrhages.

The white blood cell count was 7,400/μL with a normal differential count. The hemoglobin was 9.4 g/dL and the erythrocyte sedimentation rate was 60 mm/h. Urine analysis was unremarkable, and urine culture was negative. Four sets of blood cultures were obtained during the first 24 hours after hospital admission. Echocardiogram showed vegetations on the posterior leaflet of the mitral valve with a ruptured chordae and prolapse of the valve. Therapy was initiated intravenously with penicillin G, 2 million units every six hours and tobramycin, 100 mg two times a day.

Within 72 hours of incubation, all of the aerobic cultures in each blood culture set grew *C. pseudodiphtheriticum*. The organism was susceptible to many antibiotics by disk diffusion and minimum inhibitory concentration (MIC) determination. These antibiotics included ampicillin, MIC <0.25 μg/mL; cefamandole, MIC <0.5 μg/mL; cefoxitin, MIC <1 μg/mL; cephalothin, MIC < 0.25 μg/mL; chloramphenicol, MIC = 2 μg/mL; clindamycin, MIC <0.12 μg/mL; erythromycin, MIC <0.12 μg/mL; oxacillin, MIC <0.5 μg/mL; penicillin, MIC <0.03 μg/mL; tetracycline, MIC <1 μg/mL; and vancomycin, MIC <0.5 μg/mL. At this time, tobramycin was discontinued and intravenous penicillin G was continued at a dose of 2 million units every four hours. Blood cultures obtained on the fifth day of treatment were negative; the patient became afebrile one week after treatment was started and symptoms of CHF disappeared. The patient received a total of 28 days of penicillin therapy and has remained well since.

Discussion

The patient reported here had *Corynebacterium pseudodiphtheriticum* endocarditis proven by sustained bacteremia, identification of a vegetation on echocardiogram, and a clinical course consistent with endocarditis. He had pre-existing mitral valve disease that was probably rheumatic in origin although this is not certain; the patient was successfully treated with penicillin.

Diphtheroids infrequently cause endocarditis. It has been estimated that these organisms cause from 0.2% to 0.3% of all cases of bacterial endocarditis.[1] Prosthetic valves, rheumatic and congenital heart disease, previous or coincident endocarditis with other organisms, and valvular surgery are predisposing factors to diphtheroid endocarditis.[1,10,11] Diphtheroids show a predilection for left-sided endocarditis; this would be expected as predisposing valvular disease usually involves mitral and aortic valves. Since diphtheroids are resident flora of both the skin and nasopharynx, it appears that the primary route of infection is via the respiratory tract or from a skin source. Contamination during valvular surgery, invasive procedures such as catheterization, and intravenous drug abuse may all be sources of infection. Since this patient had no recent invasive procedure, his endocarditis was most likely caused by transient bacteremia from the normal flora of the upper respiratory tract.

Symptoms of diphtheroid endocarditis are similar to endocarditis caused by other bacteria; embolic phenomena and other signs of infective endocarditis such as splinter hemorrhages and Osler nodes have been observed. Since diphtheroids are frequent contaminants of blood cultures, the diagnosis of diphtheroid endocarditis may be difficult. It has been estimated that approximately 10% of blood cultures obtained at the Mayo Clinic are contaminated with diphtheroids.[11] In addition, blood cultures may require from five to 15 days incubation before exhibiting growth.[11] These factors, along with the low incidence of the disease, pose a challenge to the clinician in suspecting and establishing the diagnosis of diphtheroid endocarditis.

There is no uniform agreement on the antimicrobial treatment of diphtheroid endocarditis. The method of treatment most often recommended prior to the results of susceptibility testing is a combination of penicillin or erythromycin with either streptomycin or gentamicin.[10] Susceptibility of diphtheroids to antibiotics is variable, however, and this stresses the importance of in vitro antibiotic susceptibility testing.[10] In addition, a poor clinical response to antibiotics may occur in spite of in vitro susceptibility testing and an empiric change in antibiotic therapy is occasionally appropriate.

The most important prognostic factor in diphtheroid endocarditis appears to be the presence or absence of prosthetic valves. Johnson and Kaye[10] and Van Scoy and associates[11] cite a 50% mortality rate when prostheses are present. In the antibiotic era, the mortality rate in patients with natural valves ranges from 20% to 26%.[10,11]

Corynebacterium pseudodiphtheriticum, a commensal of the human nasopharynx, has been reported as an agent of endocarditis in only nine cases.[2-9] Fifty-six percent of the patients studied were between the ages of 46 and 56; 76% were men. Predisposing factors were similar to other cases of diphtheroid endocarditis. Four patients had mixed or previous endocardial infections, three had prosthetic valves, three had a history of rheumatic or other valvular lesions, two had congenital heart disease, and two had undergone recent invasive procedures. With one exception,[6] the diagnosis of endocarditis in these patients was established by a combination of multiple positive blood cultures, echocardiographic findings, or autopsy findings. Of the cases in which the involved valve was reported, all were left-sided and somewhat evenly divided between the mitral and aortic valves.

Isolates of *C. pseudodiphtheriticum* from patients with endocarditis exhibited varied antibiotic susceptibilities. In spite of treatment, however, the mortality rate associated with endocarditis caused by this organism is high. Of the nine previously reported cases, six patients died and two survived; the outcome of one patient is yet unknown.

In summary, a case of successfully treated endocarditis caused by *C. pseudodiphtheriticum* in a patient with mitral valve disease is presented. Clinicians must maintain a high index of suspicion for diphtheroid endocarditis in patients with blood cultures positive for diphtheroids since early initiation of therapy might result in a more favorable prognosis.

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Merkel cell tumor

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First identified by Toker in 1972 as trabecular carcinoma,[1] the Merkel cell tumor was until recently considered a rarity. Prior to 1984 only 53 cases had been described; now more than 100 cases have been reported. Initially only the skin is involved. However, metastases to regional lymph nodes and distant sites including bone, liver, brain, and the lungs may occur. The following report is of a case of Merkel cell carcinoma and a review of the literature.

CASE REPORT

A 67-year-old man first noticed a left supraclavicular mass in June 1983. The mass, measuring 2 cm × 1 cm, was soft, nontender, and freely moveable (Fig 1). Within the next two months several new lesions appeared and excisional biopsy of one of the masses revealed the tumor to be a Merkel cell carcinoma (Figs 2,3).

The patient's medical history included severe chronic obstructive pulmonary disease, atherosclerotic heart disease, and nephrolithiasis.

Over the next several months more than a dozen lesions appeared on the patient's skin—on the upper trunk, arms, head, neck, and groin—and ranged in size from 0.25 to 2 cm in diameter. Physical examination and work-up for metastatic disease was negative. The skin lesions were excised and biopsies were performed; all proved to be Merkel cell carcinoma. The skin lesions became too extensive for surgical therapy and the patient was started on cytotoxic chemotherapy. Treatment consisted of doxorubicin, 30 mg/m^2 (45 mg total); cyclophosphamide, 300 mg/m^2 (450 mg total); vincristine, 1 mg/m^2 (1.5 mg total); and prednisone, 40 mg daily for five days repeated every three weeks. After the second course all of the skin lesions had disappeared.

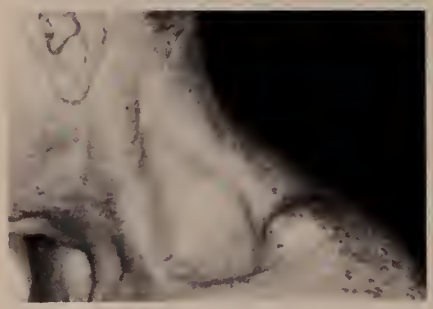

FIGURE 1. Left supraclavicular mass measuring 2 cm × 1 cm.

Chemotherapy was discontinued after the third course because of disabling acute exacerbation of the patient's chronic obstructive pulmonary disease. The patient continued to have a downhill course and five months after the initiation of chemotherapy new skin lesions appeared and the patient developed a pulmonary lesion. Fifteen months after the initial presentation the patient died. Postmortem examination revealed Merkel cell tumors of the skin and metastases to the left lung, liver, left kidney, abdominal lymph nodes, and right and left cerebellum.

DISCUSSION

Normal Merkel cells are nonkeratocytic cells found in the epidermis of mammals, although they are also present in the gingiva and palate.[2] Merkel cells are thought to function as slowly adapting mechanoreceptors mediating the sense of touch or signaling the directional movement of hairs.[3] However, not all Merkel cells are innervated and it has been proposed that Merkel cells may serve a trophic function.[2]

It has been postulated that the Merkel cell tumor is an apudoma and may originate from Merkel cells although concrete evidence to support this is lacking.[2,4-6] After observing sweat gland differentiation in two cases, Kroll and Toker believe that the cell of origin is a multipotential cell capable of both neuroendocrine and sudoriferous differentiation.[7]

In most cases of Merkel cell carcinoma lesions are found on the head, neck, and extremities. The duration of lesions prior to presentation varies from two months to two years.[2] Merkel cell tu-

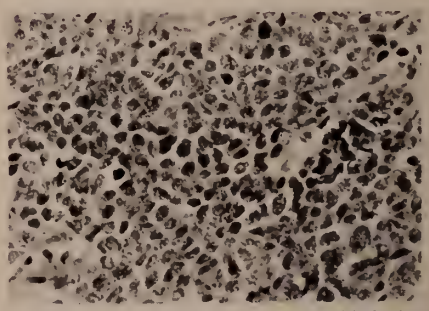

FIGURE 2. Light microscopy of the skin lesion demonstrating poorly-differentiated malignant cells of small to intermediate size with hyperchromatic nuclei, scant cytoplasm, and many mitoses. (hematoxylin and eosin stain; original magnification × 1,040)

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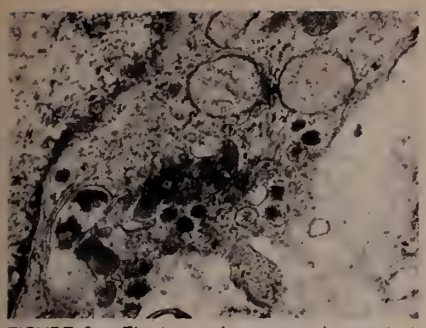

FIGURE 3. Electron microscopy demonstrating membrane-bound neurosecretory granules that are small, clustered, and of the same size. (hematoxylin and eosin stain; original magnification × 62,000)

mors may be locally aggressive and may metastasize to lymph nodes. Less often they metastasize more distantly and result in death.[7-10] Local recurrences are common and occasionally may be multiple. Metastases to the liver, lungs, bone, and brain have also been reported.[7,10] When local recurrences and metastases to regional lymph nodes occur, they usually do so within one year. However, several years may intervene before the occurrence of lymph node metastases.[2] One case of Merkel cell tumor of the forearm was reported with regional lymph node metastases occurring five years after excision of the primary lesion. This patient died of multiple metastases three years later.[4] Local recurrence does not signify that dissemination will occur. Of 30 cases reported in one study, six had distant metastases.[7] Of these six cases only four had lymph node metastases. One of the six patients had neither local recurrence nor lymph node metastases.

Merkel cell tumors are cellular and have a high mitotic rate. Invasion of adipose tissue and muscle occurs. The cell nuclei are round with dispersed chromatin and inconspicuous nucleoli. Cytoplasm is sparse. Tumor cells are arranged in sheets with scattered necrotic cells. In the study by Warner and associates the border of the tumor was infiltrative in two of six cases and pushing in three.[2]

Electron microscopy of Merkel cell tumors reveals cells containing electron-dense granules (80 to 200 nm), 10 nm filaments, and desmosomes. The electron-dense granules are of even size and usually occur in clusters, in cell processes, or beneath the cell membrane. Common features include polyribosomes, free ribosomes, and a prominent Golgi apparatus. Rough endoplasmic reticulum is sparse and the nuclei are round or oval containing finely dispersed chromatin with small eccentric nucleoli[2,3] (Fig 3).

Fine needle aspiration may aid in the diagnosis of Merkel cell carcinoma. The cells are not cohesive, the nuclei are round with well-defined nuclear membranes, mitoses are frequent, and the cytoplasm is scant.[11,12]

Gu and colleagues[8] reported that neuron-specific enolase is present in normal Merkel cells and may be used as a marker to identify Merkel cell tumors. In their study the neuron-specific enolase immunoreactivity was uniformly present in the cytoplasm of trabecular carcinoma cells that formed a rim surrounding the large, round unstained nucleus. However, in the series published by Warner and coworkers[2] neuron-specific enolase was undetected in all Merkel cell tumors.

The differential diagnosis of Merkel cell tumors includes primary and metastatic tumors of the skin such as malignant lymphomas and cutaneous metastases from oat cell carcinoma of the lung.[8] In addition, other considerations in the differential diagnosis include poorly-differentiated carcinoma, sweat gland carcinoma, medullary carcinoma, neuroblastoma, and leukemic deposits.[2]

Merkel cell tumors may be differentiated from lymphoma by the regular rounded contour of the nucleus. Large cell lymphomas have a greater irregularity of their nuclei.[3] Merkel cell tumors have scanty cytoplasm while primary malignant lymphomas of the skin are usually histiocytic and have plentiful cytoplasm.[2] Metastases of oat cell carcinoma of the lung frequently show more extensive necrosis and the cells tend to be oval in shape. The nuclei are small with clumped chromatin and the electron-dense granules may be fewer and smaller.[2,5]

The Merkel cell tumor most often has a favorable prognosis. In one study of 30 patients with Merkel cell tumor, five died from metastatic carcinoma.[7] Four of these patients in addition to excision of the tumor received radiation therapy and three also received chemotherapy. The chemotherapeutic agents employed included vincristine, doxorubicin, cyclophosphamide, and etoposide.

The recommended treatment for Merkel cell tumor is complete local excision.[2] Many patients are cured by excision, although in nearly one half of the patients lymph node metastases develop within a few years of presentation. Occasionally lymphadenopathy may be the presenting symptom. Whether prophylactic lymph node dissection should be performed is uncertain.[7]

Patients with Merkel cell tumor have been treated with radiotherapy with varying results.[3,6,7] Sidhu and colleagues reported on a 76-year-old woman who initially refused surgical resection and was treated with radiotherapy.[3] Three years later the tumor recurred at one margin of the field of radiation. DeWolf-Peeters and associates describe a patient with Merkel cell tumor with metastases to local lymph nodes who was successfully treated with radiotherapy.[6] Rapid regression following chemotherapy and radiotherapy for six to twelve months has been generally followed by recurrence.

The clinical course of Merkel cell carcinoma is usually that of a slow-growing mass that presents as a single nodule and that may recur locally or metastasize to regional nodes. However, it rarely disseminates to distant sites and rarely causes death. Of the cases discussed by Kroll and Toker in 1982[7] the outcome was favorable in most patients. Ten of 30 patients had local recurrences, 13 patients had lymph node metastases, and six patients had distant metastases, two of whom had no evidence of lymph node metastases. Twenty-three of the 30 patients were followed for more than one year at the time of publication of the data. Eleven of these were free of disease, six having had primary disease without lymph node metastases and five with lymph node metastases. Of the 11 who died, only five died from tumor related causes.

The case discussed here is illustrative of an aggressive Merkel cell carcinoma. The patient presented with one Merkel cell lesion, developed metastatic skin lesions, and later succumbed to widespread metastatic disease. Although it is rare, due to the potential severity physicians must rule out Merkel cell tumor in the differential diagnosis of cutaneous and subcutaneous nodules and cysts of the head, neck, and extremities.

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Neonatal *Hemophilus influenzae* sepsis

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Although sepsis caused by *Hemophilus influenzae* reportedly has a prevalence of 35 per 100,000 children between the ages of 6 months and 5 years,[1] its occurrence in neonates is uncommon. Precise national data are not available for *H. influenzae* sepsis; however, neonatal meningitis due to this organism occurs in only six per 100,000 live births.[2] During the period from June 1983 to June 1984, four cases of *H. influenzae* sepsis were treated in the neonatal intensive care unit at Beth Israel Medical Center in New York City. Since the authors experienced no systemic neonatal infections due to this organism in the previous two years, the following reports may carry implications for perinatal management and would be of considerable importance to practitioners in the same geographic area who treat pregnant patients and their newborns.

Case Reports

Case 1. A female infant weighing 1.2 kg was born to a 19-year-old woman after 27 weeks gestation. At birth the infant required endotracheal intubation and ventilatory support because of apnea. Antibiotic therapy was begun immediately with ampicillin 100 mg/kg/d and kanamycin 7.5 mg/kg/d. Initial white blood cell count was 4,900 /μL and platelet count was 84,000/μL. Blood cultures drawn on admission to the unit as well as a maternal cervical culture grew *H. influenzae*, growing on human blood agar plates as nonhemolytic satellite colonies of Factor V-dependent *Staphylococcus aureus* colonies. Kanamycin was discontinued after 72 hours and therapy with ampicillin was continued for 14 days, with clinical and bacteriological improvement. The infant's hospital course was complicated by hematologic abnormalities, seizures, and a grade 4 intraventricular hemorrhage with ensuing hydrocephalus that required the insertion of a ventriculoperitoneal shunt. The infant died in a chronic care facility at 6 months of age.

Case 2. A male infant weighing 1.03 kg was born after 26 weeks gestation. Endotracheal intubation was required in the delivery room because of apnea and cyanosis. A complete blood count drawn on admission to the unit showed a white blood cell count of 7,400/μL with a decreased number of platelets. Treatment with ampicillin 100 mg/kg/d and kanamycin 7.5 mg/kg/d was started at one hour of age. Cultures from the infant's blood, an eye discharge, maternal cervix, and fetal side of the placenta grew *H. influenzae*. Despite maximal ventilatory support, the infant suffered a cardiorespiratory arrest and died at 4 hours of age.

Case 3. A male infant weighing 1.17 kg was born after 28 weeks gestation to a 35-year-old mother. The infant developed severe respiratory distress by one hour of age and was treated with ampicillin 100 mg/kg/d and kanamycin 10 mg/kg/d. Initial complete blood count showed a white blood cell count of 5,500/μL with a platelet count of 18,000/μL. Despite intensive ventilatory support, the infant died four days after birth. Blood cultures drawn from the infant at the time of admission to the unit and maternal cervical cultures grew *H. influenzae*.

Case 4. A male infant weighing 2.83 kg was born at term to a 23-year-old mother. Moderate respiratory distress was noted within the first hour of life. The infant was treated with ampicillin 100 mg/kg/d and kanamycin 15 mg/kg/d. Pretreatment blood cultures from the infant grew *H. influenzae*; spinal fluid was sterile. Cultures from the maternal cervix and placenta did not grow *H. influenzae*. Initial complete blood count showed a normal white blood cell count of 26,000/μL with adequate platelets. During the first day of life the infant's respiratory status deteriorated, requiring increasing ventilatory support. The infant subsequently improved and was discharged home.

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Discussion

Although fewer than 50 cases of neonatal *H. influenzae* sepsis were reported prior to 1983, recent reports indicate an increasing prevalence of neonatal sepsis and meningitis due to that organism.[3-7] No such series has been reported, however, from this geographic area. The four infants reported here make up one half of the newborns who developed sepsis following delivery at Beth Israel Medical Center during that time period. Although the incidence of neonatal sepsis did not differ significantly from that experienced during the previous two 12-month periods, no cases of neonatal *H. influenzae* sepsis were documented during that time.

Although the individual isolates were not serotyped, a recent study by Wallace and associates[3] found a high percentage of non-typable strains isolated in neonatal systemic *H. influenzae* infections. In that study 11 of 12 (92%) isolates from Houston and an additional 19 of 24 (79%) isolates provided by the Centers for Disease Control were found to be non-typable. This overall isolation rate (83%) of non-typable strains support previous reports of increased numbers of non-typable strains of *H. influenzae* responsible for such infections.[1,3,6-8]

Several possible hypotheses have been advanced to explain this increased incidence of systemic neonatal *H. influenzae* infections. Maternal-fetal vertical transmission has already been proposed as the most likely cause of neonatal infection,[6-8] as suggested by the first three cases in this series. This transmission appears to parallel Wallace's isolation of increasing numbers of non-typable strains from both genital and neonatal sources.[3] The actual rate of carriage of this organism in the female genital tract might indeed be higher than the 1% figure suggested in the past.[3,6] Although no data are available, genital carriage rates of *H. influenzae* might be much higher in women experiencing premature labor; this association of *H. influenzae* genital colonization and prematurity has been suggested previously.[7,8]

Another possible hypothesis for the increased incidence of systemic neonatal *H. influenzae* infections is that levels of maternal or adult antibody to virulent strains of *H. influenzae* might be decreasing.[5,9] However, another report indicates that specific antibody titres to type b *H. influenzae* polysaccharide in maternal and cord serum are high.[10] No information is available, however, regarding maternal antibody levels to non-typable strains.

A third hypothesis regarding increased neonatal *H. influenzae* infections is that increased yields of *H. influenzae* may reflect improved laboratory techniques to recover this pathogen. No changes in isolation technique occurred at this hospital, however, during the study period.

The rate of such infections may also be increasing due to an evolution of the organism itself or due to the increased use of antibiotics to treat other perinatal infections. In the four cases reported on here, wide antibiotic sensitivity—including sensitivity to ampicillin, penicillin, carbenicillin, chloromycetin, tobramycin, amikacin, and moxalactam—was demonstrated. It has been previously suggested that ampicillin sensitivity may reflect that the major reservoir for these organisms is adults,[3] further strengthening the argument for vertical transmission.

A final hypothesis regarding increased *H. influenzae* infections in neonates concerns horizontal rather than vertical transmission. This may have accounted for the infections in the study reported here. In these cases, however, no two infants were treated in the unit during the same time period, eliminating the possibility of infant-to-infant nosocomial spread.

Fundamental changes in the bacterial ecology of perinatal infections continue to occur, as illustrated by the emergence of the Group B beta-hemolytic streptococcus as a major pathogen in this geographic area during the 1970s.[11] Because of the fulminant course and high mortality rate associated with that organism, the Group B streptococcus has dominated the perinatal literature on bacterial disease. This report of *H. influenzae* as a pathogen in the neonatal period should remind obstetricians, pediatricians, and neonatologists to maintain close surveillance over patterns of perinatal colonization and infection within their hospitals.

Under present methods of perinatal management, neonatal infection with *H. influenzae* carries a very poor prognosis, especially for the tiny premature infant.[7,8] Although women in premature labor might be cultured for this organism, the therapeutic implications of this strategy remain unresolved, as they do for Group B streptococcus. Early bacteremia[6,8,12] and a possible causal relationship to prematurity[7,8] strongly suggest that infection may occur prior to birth. It would seem reasonable, therefore, to administer appropriate antibiotics to all *H. influenzae* culture-positive women at risk for premature delivery and to continue antibiotic treatment in their premature infants. In light of findings of neutropenia and low percentages of mature and immature polymorphonuclear leukocytes in premature infants with *H. influenzae* sepsis,[7] strong consideration should be given to the administration of packed white cells in an effort to reduce mortality in these infants.[13] Term infants born to culture-positive women appear to have a lower infection-related mortality; such infants should be closely observed and considered possible candidates for sepsis evaluation and treatment. In three of the infants reported on here, lumbar puncture was deferred due to their unstable condition. Since neonatal *H. influenzae* meningitis has been reported by other researchers,[3,4,7,8] high-dosage ampicillin in combination with an aminoglycoside should continue to serve as the initial antimicrobial therapy pending culture reports.

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Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

Of cigarettes and sleeping pills

TO THE EDITOR: Have you taken a good look at the back cover of the July 1985 issue of the *New York State Journal of Medicine?* I did, just before I was ready to give my copy of the issue to our high school librarian for students who might use this wealth of information on cigarette smoking. The back cover shows a woman who appears to be sleeping, thanks to "#1 For Sleep." Contrary to cigarette advertising, this advertisement does not say "may be dangerous to your health." My feelings about the appropriateness of prescribing "sleeping pills" are similar to those of Dr Harvey Mandell, as expressed in his editorial "Give Him a Nytol," published in *Postgraduate Medicine*, July 1985.

Perhaps you might feel that since the *New York Times* has "refrained from editorial scrutiny of the ethics of cigarette advertisers," the *Journal* should refrain from editorial scrutiny of the ethics of the "chemical society" advertisers. Perhaps sleeping pills are not always as serious a threat to our health as cigarettes, but in some individual cases they may be a more serious and immediate threat. Realizing the threat not only to health but to life and limb which the "chemical society" poses, this advertisement for "sleeping pills" is so ominous to me that I am hesitant to present this issue to anyone without first removing the back cover. On page 468 of the same issue, the front and back covers of *Jeune Afrique* have been reproduced. When I compare this to the front and back covers of the *Journal*, it makes me wonder if you are subtly using this "sleeping pill" advertisement to demonstrate how advertising can be irresponsible.

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Cigarette smoking and quality of sperm

TO THE EDITOR: Plaudits to the *New York State Journal of Medicine* for the superb sequel issue "The World Cigarette Pandemic, Part II" (July, 1985). In further reference to the numerable effects of cigarette smoking on health, a brief communication of the results of a recent study on the quality of sperm of cigarette smokers may be of timely interest.

The effect of cigarette smoking on sperm quality as evaluated by density, motility, and morphologic abnormalities was noted in 238 age-related smokers (103 defined as having smoked ≥4 cigarettes/day over the past five years) and nonsmokers (135 defined as not having smoked for at least five years) in a blind study. Other factors that may have contributed to sperm quality were eliminated.

Spermatozoa from smokers possessed significantly decreased density and motility ($P < 0.001$) as compared with nonsmokers. Analysis of individual sperm counts indicated that there were more than twice as many smokers—77 (75%)—with a sperm density of less than 40×10^6 sperm/mL (considered to be the lower limit of the range of normal[1]) than nonsmokers—35 (26%).

Morphologic abnormalities, particularly bicephalia, appeared to be more prevalent among smokers than among nonsmokers. However, there was no significant difference ($P > 0.9$) between smokers and nonsmokers.

In view of the demonstrated presence of mutagenic properties of smoke condensates,[2] such as possessing the ability to induce sister-chromatid exchanges in peripheral blood lymphocytes,[3] it is suggested that decreases in sperm density and motility in smokers may also be reflective of smoke condensate-induced mutagenic spermatogenital alterations. The reduction of sperm motility in men who smoke may also reflect the presence of inhibitors of choline acetyltransferase that facilitates sperm motility[4] in smoke condensates.

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Molière and the smoking pandemic

TO THE EDITOR: Congratulations on your July 1985 issue of the *New York State Journal of Medicine*. It is a great step toward helping the medical profession learn how to deal with the smoking

pandemic. I would like to make a suggestion and I would also like to comment on the editor of the *Medical Journal of Australia*, Dr Alister Brass.

My suggestion is to publicize to the medical profession all of the medical journals and health magazines that are owned by the *New York Times* publishing corporation, and to encourage physicians to cancel their subscriptions to these publications. A concerted effort by enough participants could have a sobering effect on the revenues derived from these sources.

In regard to Dr Brass, I believe that as an editor he has failed on several counts to provide physicians with the truths of matters. Moreover he appears to have presented a deliberately false impression in his April 14, 1984 editorial commentary in the *MJA*, as noted in the *Journal*, on the antismoking movement in one particular reference to Molière. It is generally agreed that an editor has the right to edit materials for publication. However, to obfuscate journalism further by failing to present the whole part of an idea as it was originally written, as in the case of the quotation by Molière, is a deliberate attempt to cover up the truth, which is certainly not the right nor the province of any editor.

The quotation by Molière that Dr Brass mentions is only part of the full quotation from "Don Juan," spoken by Sganarelle, and is the following: "Quoi que puisse dire Aristote et toute la Philosophie, il n'est rien d'égal au tabac: c'est la passion des honnêtes gens, et qui vit sans tabac n'est pas digne de vivre" (Dictionnaire Des Citations Francaises, Larousse, 1977, p 394).

In analyzing the full quotation by Molière, it is clear that he was expressing the idea that despite what Aristotle and other learned persons associated with "Philosophie"—such as physicians—may say against it, tobacco is the plaything of ordinary people, and therefore he who does not live without tobacco is not worthy of living. It must be remembered that tobacco was one of the "latest things" in the time of Molière, and that he excelled at pointing out the foibles of society, and the ridiculous behavior of people trying to do all of the latest things. It is remarkable how many of Molière's comments are still valid, and go right to the core of concerns for today as well, 300 years later. It is as if Molière would be saying to us today, "Man, if you do not do cocaine, well you're just not living!"

This statement does not mean that Molière promoted either tobacco then, as Dr Brass suggests, or that he would do the same for the example given, cocaine today. However, Molière's full quotation indicates that there are people who will attempt to use such things as tobacco, no matter what the learned philosophers then, and physicians today, may say to dissuade them.

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Neonatal appendicitis

TO THE EDITOR: Acute appendicitis is rare in infants under two years of age, constituting less than 2% of cases of pediatric appendicitis.[1-4] Neonatal appendicitis is even more rare, with just over 100 cases reported in the literature.[5] Of those cases approximately 30% present as so called hernial appendicitis.[5] The following report is of a case of neonatal appendicitis occurring with hemorrhagic infarction without perforation in the hernial sac of a 13-day-old infant.

Case Report. A preterm male infant was born at 36 weeks gestation by spontaneous vaginal delivery to a 21-year-old mother with a history of drug abuse. The woman presented with premature rupture of the membranes. On delivery the amniotic fluid and placenta were foul smelling. The baby weighed 2,020 g at birth and had Apgar scores of 8 and 7. The infant's temperature was 98.4°F; heart rate, 160/min; and respiratory rate, 30/min.

Physical examination did not reveal any abnormalities and the hernial sites were normal. Laboratory investigation including complete blood count and SMA-6 were within normal limits. Examination of the cerebrospinal fluid was normal and blood cultures were negative. A right lower lobe infiltrate was seen on chest radiograph and the infant was started on gentamicin and penicillin for five days. The infiltrate resolved with the antibiotic therapy. However, on the 13th hospital day the infant was noted to have projectile vomiting. Examination revealed an incarcerated right inguinal hernia and the abdominal films showed a small bowel obstruction and air in the right inguinal region (Fig 1). Exploration performed through a right groin incision revealed a hernial sac containing a viable small bowel loop, an acutely inflamed appendix, a small amount of pus, and a discolored but viable testis. An appendectomy was performed; the appendix was 2.4 × 0.4 cm in size with discoloration and hemorrhagic infarction at the terminal 0.7 cm. There was no perforation noted. Histologic examination revealed acute suppurative appendicitis involving the tip of the appendix (Fig 2). The child made an uneventful recovery.

FIGURE 1. Abdominal radiograph showing dilated bowel loops with air in the right inguinal region.

Discussion. Although appendicitis is the most common acute surgical condition of childhood, it is extremely rare in infants and neonates. Srouji and Buck[5] reported 106 cases of acute appendicitis in neonates in a literature review from 1901 to 1975. More recently Buntain and associates[4] have cited an incidence for appendicitis in neonates to be 0.04% of all cases of childhood appendicitis. Neonatal appendicitis has been reported to occur in association with Hirschprung's disease,[6] malrotation,[1] congenital ureteropelvic junction obstruction,[7] congenital heart disease,[8] necrotizing enterocolitis,[9] and incarcerated hernia.[5,10] Neonatal appendicitis is most commonly associated with hernia. Of 94 cases reported by Srouji and Buck[5] 27 had hernial appendicitis—an incidence rate of 28.7%—whereas Buntain and coworkers[4] reported eight cases of hernial appendicitis in 67 cases of neonatal appendicitis—an incidence rate of 14%.

Rarity of neonatal appendicitis has been attributed to a number of factors such as the conical shape of the appendix,[1,11] rarity of intestinal and respiratory infections, milk and a soft-food diet, and the recumbent position of the infant.[3,12] However, if appendicitis does occur in neonates it is poorly tolerated due to a thin walled appendix, the small size of the omentum and abdominal cavity, generalized lack of physiologic

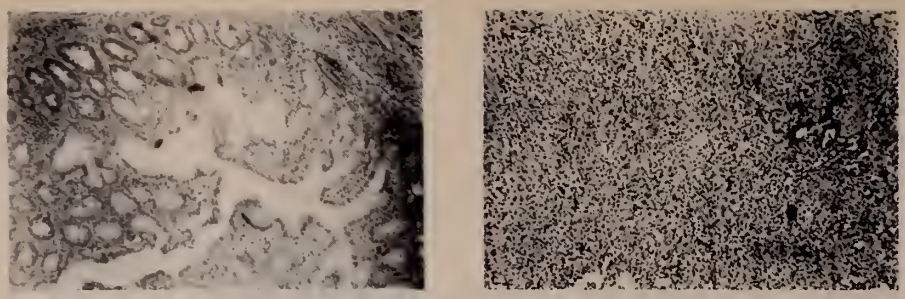

FIGURE 2. Section through normal appendix showing normal glandular structure (left). (hematoxylin and eosin stain; original magnification ×100). Section through inflamed portion of appendix showing suppurative inflammation and glandular destruction (right). (hematoxylin and eosin stain; original magnification ×100).

reserve, prematurity, and vague symptoms that lead to a delay in diagnosis.[5,10,13] Perforation and delayed treatment are the two most important factors leading to high mortality from neonatal appendicitis.[4]

In contrast, hernial appendicitis carries a better prognosis than neonatal appendicitis. The diagnosis is made more easily and quickly due to early operation for incarcerated hernia.[5] Another reason that hernial appendicitis has a better prognosis than neonatal appendicitis is that the process is isolated in the hernial sac by the shielding of the peritoneal cavity.[5] The incidence of perforation in hernial appendicitis is low compared to that of abdominal appendicitis. Srouji and Buck[5] report an incidence of perforation in eight of 27 cases (29.6%) of hernial appendicitis whereas 42 of 67 cases of abdominal appendicitis (62.6%) had perforation. Buntain and associates[4] reported the incidence of perforation in intraabdominal appendicitis to be 76%. An even higher incidence of perforation has been reported in other series[1,14] for intraabdominal appendicitis.

Appendicitis has also been seen with hernia without incarceration.[5] However, it has not been established what caused the appendicitis in these cases. In the case of incarcerated hernia the appendicitis is most likely caused by the direct pressure of the hernial contents on the appendix thereby obstructing the lumen or the arterial supply and leading to hemorrhagic infarction.[5] This appears to be the cause of appendicitis in the case presented here.

The prognosis is excellent in hernial appendicitis and no mortality has been reported as yet. However, a high index of suspicion and early treatment is warranted for intraabdominal appendicitis.

Acknowledgments. The authors thank Elaine Estuita, MD, Department of Pathology, and Mr P. Archibald, Department of Photography, for their assistance.

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EXERCISE AND SPORTS SCIENCES REVIEWS

Edited by Ronald L. Terjung, PhD. 596 pp, illustrated. New York, Macmillan Publishing Co, 1985. $29.95 (hardcover)

This volume consists of a number of research reviews from the clinical, biochemical, biomechanical, behavioral, and psychologic aspects of exercise science. The contributors are recognized authorities in their specific fields. The stated purpose of the book is to maintain and extend the breadth and depth of current reviews in the general areas of interest to practitioners, students, and exercise scientists.

The book's contents consist of 14 papers that may be classified as follows: biochemistry (1), biomechanics (4), rehabilitation (2), physiology (4), psychology (2), and growth and development (1). The biochemical topic deals with the hepatic regulation of glucose during exercise and is a current synopsis of this subject, although it has little clinical utility. The subsequent four papers deal with various physiology topics including exercise-induced fluid shifts, oxygen transport capacity, and muscle blood flow and energetics. The paper on transport capacity and aerobic performance is of particular merit as it coherently reviews the perplexing issue of sports anemia and the timely, albeit heated question of blood doping. The discussion of the physiologic changes within fluid compartments occurring during short-term, intermediate, and long-term exercise is extremely useful for both the sports physiologist and the clinical sports medicine specialist. Fluid and electrolyte requirements are discussed for a variety of training protocols and environmental situations. The biomechanical contents of the text range from the neurophysiologic concerns of movements and the acquisition of skills to the mechanical properties of muscle and the biomechanics of running. The latter paper clearly and concisely discusses the kinematics of running and the various elements of the athlete's foot, the type of foot gear, and the track conditions. The basic science format is readily transferable to the clinical situation. On the other hand, the chapter on skill acquisition through augmented information deals with some new concepts of biofeedback and related learning theory. Although much of the information is not readily applicable to the clinician, the future of such approaches is seemingly bright.

The two rehabilitation chapters dealing with spinal cord injuries and the child with cardiorespiratory disease represent a balanced synthesis of basic science and clinical material. A variety of different exercise programs are discussed and their effects on aerobic power, a variety of metabolic parameters, and their long-term impact on risk factors are succinctly detailed. Psychological issues discussed in two papers deal with compliance and sports subcultures, respectively. Certainly, there is a no more frustrating area in exercise and physical training than adherence to a training program. The different types of problems one commonly encounters in compliance and their possible solutions through behavior modification and social support factors are nicely detailed in the compliance chapter. The sports subcultures paper provides further insight into these factors by relatther insight into these factors by relating uniformity of class, gender, age, race/ethnicity, and geographical reference to the choice of physical activity or sport. Such activities gain meaning through the social reproduction and transformation of its participant membership. Thus, not uncommonly, a sports prototype emerges that embodies the type of person who is a successful participant and who epitomizes a successful outcome.

The last paper in the text concerning the developmental aspects of athletics deals with the aerobic capacity of children. This is a relatively new area of research in exercise physiology and is characterized by problems inherent in of training. The simultaneous effects of maturation, growth, and development often compound any intervention being studied. Nonetheless, this paper goes far in elucidating the effects of training in children, their standardization, and future research prospects.

This volume of *Exercise and Sports Sciences Reviews* is a solid addition to an authoritative sports medicine series. Because of the detailed nature of many of the articles in the text, it is not recommended for the casual devotee of sports medicine, nor for individuals interested solely in the clinical aspects of primary care sports medicine. The book is recommended for individuals who are deeply involved in research concerning various sports medicine topics and who are interested in the basic science aspects of sports physiology. The concise scientific language and well-developed organization of the book are clearly designed to meet the needs of this latter group.

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ARTHROSCOPY OF THE KNEE. A DIAGNOSTIC COLOR ATLAS

By David J. Dandy, FRCS. 159 pp, illustrated. Philadelphia, Lea & Febiger, 1984. $44.00 (hardcover)

In the past ten years the specialty of orthopedic surgery has changed dramatically, both in its basic concepts and in practice by the introduction of arthroscopy. Few people are more qualified than Dandy to describe this topic.

No serious arthroscopist can afford not to read this diagnostic color atlas and to share in the author's perspective of normal and pathological anatomy. The text examines the normal knee, synovial disorders, bone and cartilage disorders, ligament lesions, and the damaged meniscus in a systematic fashion. If there can be any negative criticism of this book, it is that the evaluation of normal anatomy is too thorough.

The author takes the reader step by step through the arthroscopic appearance of the knee. Each individual step

consists of four parts. The first is a written text describing the actual arthroscopic appearance which like the second part is beautifully reproduced pictorially. The third part is a line diagram that is accompanied by the color photographs. This includes not only the artist's representation of the visual field, but also of the surrounding anatomy in an attempt to orient the reader. The fourth part is a panel that includes a sketch of the knee showing instrument placement.

I have had the opportunity of hearing several reports given by the author and of listening to his hypotheses concerning diseases of the knee. They are very logical and extremely valuable, and this work with its observations and comments is more than a complement to them. No doubt the absence of references will be criticized by some, but as the author states, the body of knowledge relating to arthroscopic anatomy is still too small to be authoritative. I believe the next generation will look back to Dandy as a major contributor and this text as a major education aide to the advancement of knowledge of knee disease. I recommend this book as must reading for both the novice and experienced arthroscopist.

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THE VALUE OF PREVENTIVE MEDICINE

By Ciba Foundation Symposium 110. 258 pp, illustrated. London, Pitman Books, 1985. $35.00 (hardcover)

Preventive medicine has been proclaimed by some to be the solution to the problem of escalating costs of medical care. Politicians in particular have looked favorably on preventive medicine programs, sometimes without adequate critical analysis, as a means of reducing medical costs. Practitioners of alternative forms of medical care usually stress the preventive aspects and imply that other practitioners are not interested in preventive medicine. This Ciba Foundation Symposium attended by a carefully selected group of experts—physicians, epidemiologists, health economists, and medical sociologists from several countries—documents the evidence presently available for determining the value of most recognized preventive measures.

The symposium opens with a provocative paper on the objectives of preventive medicine by Sir Richard Doll in which the need in developed countries for prevention of cardiovascular disease and cancer is stressed. Doll also focuses on many of the problems of prevention. Next, the economic aspects of prevention are discussed by Bengt Jönsson of Sweden who indicates the importance of considering willingness to pay for both private benefits and social benefits in any economic evaluation system. These introductory papers are followed by presentations covering most major topics in preventive medicine. D. J. Weatherall discusses genetic screening; Jeffrey P. Koplan, immunization programs; T. W. Meade, screening for hypertension and heart disease; David M. Eddy, screening for cancer; Ingvar Hjermann, risk factor intervention in coronary heart disease; Richard Peto, tobacco-related disease; Bo Petersson and associates, alcohol-related disease; and Roy J. Shephard, the value of physical fitness. There are two papers that focus on methods of improving the scientific evaluation of preventive medicine measures, one by Geoffrey Rose is on controlled trials, and the other by Louise B. Russell is on the design of future studies. The final paper by Howard H. Hiatt and Milton C. Weinstein raises the all-important issue of assigning priorities for programs of medical care and recommends giving a higher priority to preventive medicine.

In a topic as controversial as preventive medicine, it is difficult to bring out all of the viewpoints in the papers themselves. This deficiency is corrected in the lively and uninhibited discussions that follow each paper. As a result, the symposium presents an authoritative and balanced view of preventive medicine today. We are left with the impression that physicians do have a real interest in practicing preventive medicine and in improving it. However, much remains to be done in order to be certain that available methods are effective and worth the cost.

The book is of convenient size, and is well edited. I would recommend it for all those interested in preventive medicine, laymen as well as physicians, and especially for those involved in governmental policy decisions.

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COMPREHENSIVE MANAGEMENT OF RESPIRATORY EMERGENCIES

Edited by Barry E. Brenner, MD. 398 pp, illustrated. Rockville, MD, Aspen Publications, 1985. $61.50 (hardcover)

When I received this book to review, I was excited that a new addition to the literature was here; specifically, a text devoted to the management of respiratory emergencies. As a lung specialist, I was disappointed because the text does not sufficiently deal with enough pulmonary emergencies. As a matter of fact, of the 20 chapters and 386 pages, probably only 100 pages cover what comprise true respiratory emergencies. Thus the text could have been considerably shorter, with the editor and contributors avoiding the publication of another text book on pulmonary medicine.

The text is well written and has a very thorough, updated bibliography (as recent as 1983) of nearly 2,500 citations. It is a graphic book with over 150 tables, figures, and roentgenograms. I was pleased with the handling of several chapters. The chapter on the emergency management of neonatal disorders is excellent as is the presentation of acid-base abnormalities. The chapter on management of asthma is also excellent, and there are good sections on blunt chest trauma, cardiogenic pulmonary edema, toxic gas and inhalation injuries, pulmonary embolism, and hemoptysis. Carbon monoxide poisoning is thoroughly reviewed by one of the contributing editors.

Several chapters are inadequate for a text entitled *Comprehensive Management of Respiratory Emergencies*; these include chest radiology and respiratory failure. I believe a more in-depth discussion of the topics covered on chest radiology would have been in order. Oxygen therapy was not covered well in the chapter on respiratory failure, although a separate chapter on oxygen therapy is included at the end of the text. Unfortunately, even in this final chapter there were repeated errors in listing the Fio_2 as a percentage, instead of as a fraction. The section on mechanical ventilators is superficial and too opinionated for a textbook. For example, the statement "intermittent mandatory ventilation is the widely preferred ventilatory mode" should have been avoided. The authors mention high frequency ventilation, but do not adequately discuss its role in tracheobronchial disruption as it pertains to

respiratory emergencies. It would have been welcome to see a section on how ventilators may be used for true emergencies, such as moribund status asthmaticus.

In summary, I believe that the editor and contributors have put together a satisfactory text on pulmonary medicine. The book would have served the function of the title if it were half the length and dealt with true respiratory emergencies. I would not then have been disappointed. At present, I believe $61 for this book is too much for too little on the intended subject.

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EMERGENCY PROBLEMS IN THE ELDERLY

Edited by Edward P. Hoffer, MD. 256 pp, illustrated. Oradell, NJ, Medical Economics Books, 1985. $22.95 (hardcover)

This book originated from a symposium, "Emergency Problems in the Elderly," held in Boston in 1983. It's aim is to outline the pathophysiology and treatment of various types of emergencies that occur in the older adult. The editor's goal was not to produce an exhaustive text but rather one that provides readers with a quick review of approaches to problems seen in either an emergency room, nursing home, or in the physician's office. The various contributors to the book (speakers at the symposium) are individuals who have had extensive experience with the care of older adults.

The text offers useful and valuable brief summaries of various emergencies that are commonly seen. Chapter structure permits the reader to review various problems as they are encountered. It is interesting to note that instead of focusing on a particular organ system, as do so many texts, this book is more symptomatically oriented. This helps readers through a realistic multisystem differential diagnosis.

Areas included in this text are pulmonary emergencies, evaluation of chest pain, acute abdominal pain, and gastrointestinal bleeding. There are other sections devoted to urinary retention, diabetic emergencies, hypothyroidism, fever, psychiatric emergencies, and approaches to coma and altered status of consciousness. The final chapter in the book deals with a topic rarely addressed in other geriatric tests, namely that of abuse and neglect. The authors of this chapter not only include the obvious signs of physical abuse but also list other types of abuse that occur in the elderly.

This book is clearly written in very concise language. It will appeal to physicians, nurses, and other health care professionals who work in emergency treatment situations. Each section includes suggestions on various diagnostic tests that aid in caring for individual patients. There are also helpful treatment suggestions. The general organization of the book is such that information can be easily found.

This book is highly recommended to health care professionals who care for the older adult. Even though the information in some selected areas is slightly out of date, it may certainly be used in emergency rooms and offices as a quick reference.

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LABAT'S REGIONAL ANESTHESIA: TECHNIQUES AND CLINICAL APPLICATIONS

Fourth Edition. Edited by John Adriani, MD. 600 pp, illustrated. St. Louis, MO, Warren H. Green, Inc., 1984. $58.75 (hardcover)

The resurgence of interest in regional anesthetic techniques makes the publication of the fourth edition of *Labat's Regional Anesthesia* a timely one. This book is of historical interest in that the first edition was published in 1922. In fact, the basic principles and techniques as originally described by Labat are presented intact here. By updating and expanding the original work, John Adriani, MD, has attempted to preserve the character of this classic volume while covering the fundamental aspects of present day regional anesthetic practice.

The work is organized into introductory chapters on the pharmacology of local anesthetic agents and general principles of neural blockade. Subsequent chapters, organized by specific anatomic regions, describe blocks applicable to surgical procedures in those regions. There is a short chapter on diagnostic and therapeutic neural blockade, a chapter on topical anesthesia, and a final short chapter on the early history of regional anesthesia.

Unfortunately, the work is very uneven. A great deal has been learned about the pharmacodynamics and pharmacokinetics of local anesthetic agents over the years; their treatment here is cursory and not well referenced. The use of intrathecal and epidural narcotics and the diagnosis and treatment of chronic pain syndromes, two of the newer and most promising applications of regional anesthesia, receive limited attention. On the other hand, the chapters entitled "Blockade of Cranial Nerves" and "Operations on the Head" are excellent with both concise descriptions and detailed drawings. The chapter on spinal anesthesia contains detailed and informative drawings but provides only cookbook-like instructions as to the conduct of a safe spinal anesthetic with no discussion of the pertinent physiology. The chapter on epidural anesthesia covers the basics. However, a more thorough treatment of its effects and the maternal-fetal unit would be welcome. Finally, the chapter on the early history of regional anesthesia provides the reader with a concise overview of the topic.

The editor has taken on a very difficult task. The book has retained the flavor of Labat's original work but is lacking as a comprehensive overview of modern regional anesthesia. Those seeking such a comprehensive, well referenced text would be better served by the purchase of *Neural Blockade: In Clinical Anesthesia and Management of Pain* by Cousins and Bridenbaugh.

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In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Nathan Artsis, MD, Merrick. Died November 1, 1985; age 78. Dr Artsis was a 1932 graduate of Hahnemann Medical College and Hospital of Philadelphia. He was a member of the American Academy of Family Physicians, the Nassau County Medical Society and the Medical Society of the State of New York.

Gunter J. Bach, MD, Rochester. Died October 3, 1985; age 71. He was a 1939 graduate of Universität Basel Medizinische Fakultät. Dr Bach was a Diplomate of the American Board of Family Practice and a member of the Academy of Medicine, the American Academy of Family Practice, the Medical Society of the County of Monroe and the Medical Society of the State of New York.

James Vincent Barrett, MD, Averill Park. Died November 14, 1985; age 75. Dr Barrett was a 1933 graduate of Albany Medical College of Union University. He was a member of the American Academy of Family Practice, the Medical Society of the County of Rensselaer and the Medical Society of the State of New York.

Nehoray Boghrati, MD, Laguna Beach, California. Died November 1, 1985; age 73. Dr Boghrati was a 1936 graduate of the Université de Paris Faculté de Médecine. Dr Boghrati was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Edward Riley Cannon, MD, Cazenovia. Died August 30, 1985; age 74. Dr Cannon was a 1940 graduate of the University of Buffalo School of Medicine. He was a member of the Medical Society of the County of Madison and the Medical Society of the State of New York.

Anthony Richard Costa, MD, Staten Island. Died October 9, 1985; age 41. Dr Costa was a 1971 graduate of the New Jersey College of Medicine and Dentistry. He was a Diplomate of the American Board of Orthopedic Surgery and a member of the American Academy of Orthopaedic Surgeons, the Richmond County Medical Society and the Medical Society of the State of New York.

Willard John Davies, MD, Rockville Centre. Died November 4, 1985; age 84. He was a 1927 graduate of the University of Pennsylvania School of Medicine. Dr Davies was a Fellow of the American College of Physicians and the American College of Chest Physicians. His memberships included the Academy of Medicine, the New York State Society of Internal Medicine, the International Society of Internal Medicine, the American Thoracic Society, the Nassau County Medical Society and the Medical Society of the State of New York.

John Daniel Diorio, MD, Schenectady. Died May 26, 1985; age 68. Dr Diorio was a 1943 graduate of the University of Maryland School of Medicine. Dr Diorio was a member of the Medical Society of the County of Schenectady and the Medical Society of the State of New York.

Samuel Anthony Dispenza, MD, Jamestown. Died October 15, 1985; age 75. Dr Dispenza was a 1937 graduate of the University of Buffalo School of Medicine. He was a Fellow of the American Academy of Family Physicians, the Medical Society of the County of Chautauqua and the Medical Society of the State of New York.

John Thomas Donovan, MD, Columbus, North Carolina. Died November 4, 1985; age 67. Dr Donovan was a 1943 graduate of the University of Buffalo School of Medicine. He was a Diplomate of the American Board of Radiology and a member of the Academy of Medicine, the Radiological Society of North America, Inc., the Medical Society of the County of Niagara and the Medical Society of the State of New York.

Nathan E. Finkelstein, MD, Nanuet. Died October 21, 1985; age 81. Dr Finkelstein was a 1934 graduate of Universität Bern Medizinische Fakultät. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Charles Friedman, MD, Fishkill. Died September 24, 1985; age 73. Dr Friedman was a 1942 graduate of the American University of Beirut School of Medicine. He was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Surgery, the Dutchess County Medical Society and the Medical Society of the State of New York.

Jacob Frumkin, MD, Schenectady. Died August 24, 1985; age 80. He was a 1931 graduate of Albany Medical College of Union University. Dr Frumkin was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Urology. His memberships included the American Urological Association, the Medical Society of the County of Schenectady and the Medical Society of the State of New York.

Morris Isaiah Gerner, MD, Chester. Died October 19, 1985; age 78. He was a 1933 graduate of the University of Wisconsin Medical School. Dr Gerner was a Fellow of the American Academy of Family Practice, a Diplomate of the American Board of Family Practice, and a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

Leonard B. Ginsburg, MD, Suffern. Died September 27, 1985; age 71. He was a 1941 graduate of the Université de Lausanne Faculté de Médecine. Dr Ginsburg was a Diplomate of the American Board of Radiology and a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

John Patrick Grogan, MD, Slingerlands. Died October 19, 1985; age 53. He was a 1958 graduate of Albany Medical College of Union University. Dr Grogan was a Diplomate of the American Board of Family Practice and a member of the American Academy of Family Practice, the Medical Society of the County of Albany and the Medical Society of the State of New York.

Saul Isaac Heller, MD, New York. Died November 18, 1985; age 80. He was a 1929 graduate of Cornell University Medical College. Dr Heller was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Academy of Neurology, the American Psychiatric Association, the Pan American Medical Association, the Association for Research in Nervous and Mental Disease, the New York County Medical Society and the Medical Society of the State of New York.

Roy Frederick Herrman, MD, Marietta, Ohio. Died October 29, 1985; age 83. Dr Herrman was a 1928 graduate of Rush Medical College, Chicago. He was a member of the Academy of Medicine, the Medical Society of the County of Monroe and the Medical Society of the State of New York.

Eleanor Ann Intagliata, MD, Brooklyn. Died November 15, 1985; age 58. She was a 1956 graduate of Università Degli Studi di Roma, Facoltà di Medicina e Chirurgia. Dr Intagliata was a Diplomate of the American Board of Anesthesiology and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the New York County Medical Society and the Medical Society of the State of New York.

Gustav Jellinek, MD, New York. Died November 23, 1985; age 100. Dr Jellinek was a 1911 graduate of Medizinische Fakultät der Universität, Wien. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Robert P. Jessup, MD, Mattituck. Died November 12, 1985; age 68. He was a 1943 graduate of the State University of New York Downstate Medical Center. Dr Jessup was a member of the Academy of Medicine, the American Occupational Medical Association, the American Academy of Occupational Medicine, the Nassau County Medical Society and the Medical Society of the State of New York.

Jacob I. Lampert, MD, Williamsville. Died September 20, 1985; age 78. He was a 1930 graduate of the University of Buffalo School of Medicine. Dr Lampert was a member of the Academy of Medicine, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Herbert Lansky, MD, Buffalo. Died September 29, 1985; age 60. He was a 1949 graduate of the University of Buffalo School of Medicine. Dr Lansky was a Fellow of the American College of Pathologists and a Diplomate of the American Board of Pathology. His memberships included the New York State Society of Pathologists, the American Society of Clinical Pathologists, the International Academy of Pathology, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Joseph J. La Vine, MD, Baldwin. Died November 18, 1985; age 83. Dr La Vine was a Diplomate of the American Board of Radiology. He was a member of the Radiological Society of New York State, the New York Roentgen Society, the Nassau County Medical Society and the Medical Society of the State of New York.

Kyoo Hyun Lee, MD, Howard Beach. Died November 14, 1985; age 41. Dr Lee was a 1968 graduate of Seoul National University College of Medicine. Dr Lee was a member of the American Academy of Physical Medicine and Rehabilitation, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Samuel Leibowitz, MD, Brooklyn. Died November 22, 1985; age 76. He was a 1937 graduate of Medizinische Fakultät der Universität, Wien. Dr Leibowitz was a Fellow of the American College of Chest Physicians and a member of the New York State Society of Internal Medicine, the American Geriatrics Society, the American Thoracic Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Phelps Paul Luria, MD, Cedarhurst. Died September 24, 1985; age 71. He was a 1940 graduate of the University of Western Ontario. Dr Luria was a Qualified Fellow of the International College of Surgeons and a Diplomate of the American Board of Otolaryngology. His memberships included the American Academy of Otolaryngology, the American Academy of Facial Plastic and Reconstructive Surgery, the American Geriatrics Society, the Medical Society of the County of Queens and the Medical Society of the State of New York.

William Edward Mathews, MD, Niagara Falls. Died September 30, 1985; age 85. He was a 1927 graduate of the University of Cincinnati College of Medicine. Dr Mathews was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons. He was a member of the Academy of Medicine, the Medical Society of the County of Niagara and the Medical Society of the State of New York.

Edward Burnard McCabe, MD, Norfolk, Connecticut. Died July 20, 1985; age 68. He was a 1944 graduate of Jefferson Medical College of Philadelphia. Dr McCabe was a Diplomate of the American Board of Radiology and a member of the Medical Society of the County of Schenectady and the Medical Society of the State of New York.

Lester Lynn Merrits, MD, Mineola. Died October 3, 1985; age 44. He was a 1965 graduate of Università Degli Studi di Bologna, Facoltà di Medicina e Chirurgia. Dr Merrits was a Fellow of the American College of Cardiology and a Diplomate of the American Board of Internal Medicine. His membershps included the New York State Society of Internal Medicine, the Nassau County Medical Society and the Medical Society of the State of New York.

Frank D. Napolitani, MD, Mahopac Falls. Died August 3, 1985; age 77. He was a 1939 graduate of Middlesex University School of Medicine, Waltham. Dr Napolitani was a Fellow of the American College of Obstetricians and Gynecologists and a member of the Academy of Medicine, the American Geriatrics Society, the Pan American Medical Association, the Bronx County Medical Society and the Medical Society of the State of New York.

Roland Peter Nesi, MD, Brooklyn. Died November 12, 1985; age 80. Dr Nesi was a 1933 graduate of Università De-

gli Studi di Roma, Facoltà di Medicina e Chirurgia. He was a member of the American Academy of Family Physicians, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Toula G. Panay, MD, New York. Died October 22, 1985; age 68. Dr Panay was a 1947 graduate of National and Capodestrian University Faculty of Medicine, Athens. Dr Panay was a Fellow of the American College of Obstetricians and Gynecologists, a Diplomate of the American Board of Obstetrics and Gynecology, and a member of the New York County Medical Society and the Medical Society of the State of New York.

John S. Paroski, MD, North Tonawanda. Died September 19, 1985; age 31. Dr Paroski was a 1980 graduate of the University of Buffalo School of Medicine. He was a member of the American Academy of Pediatrics, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Marcello Petraroja, MD, Brooklyn. Died June 1985; age 87. He was a 1923 graduate of Università di Napoli Facoltà di Medicina e Chirurgia. Dr Petraroja was a member of the American Academy of Family Physicians, the American Geriatrics Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Guido S. Ramos, MD, Guttenberg, New Jersey. Died October 5, 1985; age 55. Dr Ramos was a 1957 graduate of Universidad de la Habana Facultad de Medicina y Farmacia. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Henry C. Rhein, MD, Far Rockaway. Died November 2, 1985; age 62. Dr Rhein was a 1949 graduate of the St. Louis University School of Medicine. He was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Seymour M. Schoenholz, MD, Campbell Hall. Died October 6, 1985; age 78. Dr Schoenholz was a 1933 graduate of the University of St. Andrews Conjoint Medical School. He was a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

Jacob Schnitman, MD, Valhalla. Died October 18, 1985; age 74. Dr Schnitman was a 1936 graduate of Universität Basel Medizinische Fakultät. He was a member of the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Nathan A. Solomon, MD, Brooklyn. Died September 3, 1985; age 63. He was a 1959 graduate of State University of New York Downstate Medical Center. Dr Solomon was a Diplomate of the American Board of Nuclear Medicine and a member of the Society of Nuclear Medicine, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Henry Martin Taterka, MD, New York. Died November 18, 1985; age 87. He was a 1922 graduate of Schlesische-Friedrich-Wilhelms Universität Medizinische Fakultät, Breslau. Dr Taterka was a Diplomate of the American Board of Radiology and a member of the New York Roentgen Society, the Radiological Society of North America, Inc., the New York County Medical Society and the Medical Society of the State of New York.

Jules Warren Toff, MD, New York. Died November 20, 1985; age 67. He was a 1956 graduate of Université de Geneve Faculté de Medecine. Dr Toff was a Fellow of the American College of Preventive Medicine and a Diplomate of the American Board of Preventive Medicine, Inc. His memberships included the Academy of Medicine, the American Public Health Association, the Pan American Medical Association, the Bronx County Medical Society and the Medical Society of the State of New York.

Dominic R. Trozze, MD, Binghamton. Died October 13, 1985; age 77. He was a 1936 graduate of Université de Geneve Faculté de Medecine. Dr Trozze was a member of New York State Society of Anesthesiologists, the Academy of Medicine, the American Society of Anesthesiologists, Inc., the Broome County Medical Society and the Medical Society of the State of New York.

Robert M. Weiss, MD, Poughkeepsie. Died November 21, 1985; age 57. He was a 1951 graduate of the State University of New York Downstate Medical Center. Dr Weiss was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Neurological Surgery. His memberships included the New York Society of Neurosurgery, the American Association of Neurological Surgeons, the Dutchess County Medical Society and the Medical Society of the State of New York.

Margaret L. Williams, MD, Syracuse. Died August 14, 1985; age 62. She was a 1949 graduate of the University of Pennsylvania School of Medicine. Dr Williams was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the American Pediatric Society, the Onondaga Medical Society and the Medical Society of the State of New York.

James Isadore Yanick, MD, Hornell. Died November 15, 1985; age 82. Dr Yanick was a 1928 graduate of Cornell University Medical College. He was a member of the Steuben County Medical Society and the Medical Society of the State of New York.

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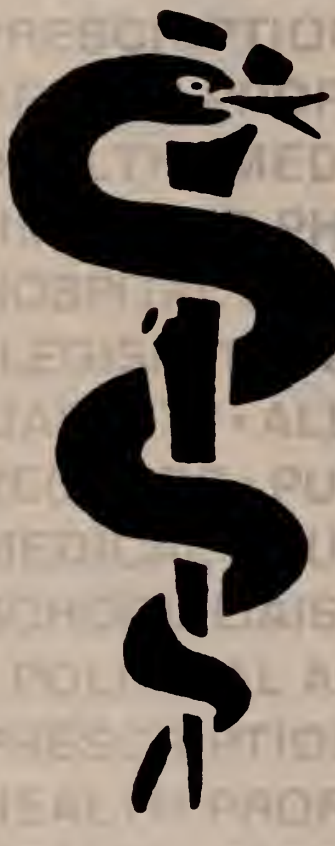
NYMPAC



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ANNUAL CME ASSEMBLY

Maintaining the Quality of
Health Care into the 21st Century.

March 7–9, 1986

and the

Annual Meeting of the House of Delegates March 6–9, 1986

The New York Hilton
New York City

COURTESY N.Y. CONVENTION & VISITORS BUREAU

HIGHLIGHTS . . .

- 22 Sessions
- Panel Discussions
- Technical Exhibits
- President's Dinner Dance

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NOTE: Reservations must be received no later than February 13, 1986 and will be held only until 6 p.m. on day of arrival unless later hour is specified.

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ARRIVAL DATE _____

☐ 2-4 p.m. ☐ 4-6 p.m. ☐ 6-8 p.m. ☐ after 8 p.m.

DEPARTURE DATE _____

(checkout time is 1 p.m.)

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MEDICAL SOCIETY OF THE STATE OF NEW YORK
Annual Meeting of the House of Delegates
March 6-9, 1986
Annual CME Assembly
March 7-9, 1986

Circle preferred rate:

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GENERAL INFORMATION

The Medical Society of the State of New York invites you to attend its 1986 Annual CME Assembly to be held March 7–9, at the New York Hilton. The Continuing Medical Education Sessions and Technical Exhibits are open to all physicians, their guests and the allied professions. The two and a half days of meetings will provide the individual physician with a possible 18 credits out of a total of 93 Category 1, CME credit hours being offered. Over 120 outstanding speakers, including a number from out-of-state, will present papers at 22 sessions.

The theme of the CME Sessions will be "Maintaining The Quality of Health Care Into The 21st Century." A few of the subjects to be presented are, Alcoholism and Gastroenterology; Realistic Uses of Computers in Medical Practice; Evaluation and Management of Temporal Mandibular Joint Disorders; Laser Therapy in Urogenital Disorders; and An Overview of Geriatric Psychiatry. For details, see the Preliminary Program which appears in the December 1985 issue of the *New York State Journal of Medicine*. Our program will offer the clinician new approaches in diagnosis and treatment of diseases in a wide range of medical specialties.

COURTESY NEW YORK CONVENTION AND VISITORS BUREAU

MUSEUM OF MODERN ART SCULPTURE GARDEN

Comments from attendees at the 1985 CME Assembly were: 'The Speakers are excellent and well-informed'; 'The presentation was timely, and the material was well illustrated'; 'My time was well spent'. Don't miss this opportunity to gain Category 1 credits over a weekend when you are free from office hours. Why not bring your family. There is no registration fee for MSSNY members. Professional representatives from more than 50 companies will be in the Rhinelander Gallery Exhibit Hall to discuss their products and services. The Technical Exhibits will include drug products, clinical laboratories, office equipment, computer services, educational, insurance protection, and financial services, career opportunities and more.

SPECIAL EVENTS

Thursday, March 6

The Annual Dinner Dance will be held in the Trianon Ballroom of the New York Hilton, in honor of Daniel F. O'Keeffe, M.D., President, preceded by a reception in the Mercury Ballroom at 7:00 p.m. All attendees are welcome. Tickets are $75.00 per person and should be ordered in advance from the Medical Society.

Friday, March 7 and Saturday, March 8

A reception for physicians, their guests, the allied professions and exhibitors will be held on both days in the Exhibit Hall between 5:00 p.m. and 6:00 p.m., compliments of the Medical Society of the State of New York. A free drawing for a color TV set will take place at both receptions.

HOTEL RESERVATIONS

Physicians must make their own reservations with the New York Hilton no later than February 13, 1986. After that date, rooms are on an availability basis only. If making reservations by telephone, please mention that you are attending the Medical Society Convention for billing at the special rate.

REGISTRATION

CME Registration will take place in the Rhinelander Gallery Exhibit Hall, located on the 2nd floor which is accessible by escalators from the lobby. Friday, March 7 and Saturday, March 8 from 8:30 a.m. to 5:00 p.m.; Sunday, March 9 from 8:30 a.m. to 12:30 p.m.

House of Delegates Registration will take place on the 2nd and 3rd floor promenades at the following hours: Wednesday, March 5, from 12 Noon to 7:30 p.m.; Thursday, March 6, Friday, March 7 and Saturday, March 8, from 8:30 a.m. to 5:30 p.m. and Sunday, March 9 from 8:30 a.m. to 12 Noon. All MSSNY members are welcome.

CME MEETING HOURS

Friday, March 7 —10 a.m.–1 p.m.
2 p.m.–5 p.m.

Saturday, March 8—10 a.m.–1 p.m.
2 p.m.–5 p.m.

Sunday, March 9 —10 a.m.–1 p.m.

EXHIBIT HOURS

Friday, March 7 —9 a.m.–11 a.m.
1 p.m.–6 p.m.

Saturday, March 8—9 a.m.–11 a.m.
1 p.m.–6 p.m.

Sunday, March 9 —9 a.m.–1 p.m.

1986 ANNUAL CME ASSEMBLY

Medical Society of the State of New York
New York Hilton, New York City

Maintaining the Quality of
Health Care into the 21st Century

FRIDAY, MARCH 7

10:00 a.m. 1:00 p.m.
Cardiovascular Diseases, *Beekman Parlor*
Gastroenterology/Alcoholism, *Sutton Parlor North*
Obstetrics/Gynecology, *Sutton Parlor Center*
Neurosurgery, *Sutton Parlor South*
Physical Medicine & Rehabilitation, *Regent Parlor*
Update on AIDS, *Morgan Suite*

2:00 p.m. - 5:00 p.m.
Neurology, *Beekman Parlor*
Pediatrics/Alcoholism, *Sutton Parlor North*
Chest Diseases, *Sutton Parlor Center*
Occupational & Environmental Health/Workers Comp., *Sutton Parlor South*
Medical Liability Mutual Insurance Co., *Regent Parlor*
Realistic Uses of Computers in Medical Practice, I, *Madison Suite*

SATURDAY, MARCH 8

10:00 a.m. 1:00 p.m.
Ophthalmology (All Day), *Beekman Parlor*
Internal Medicine (All Day), *Sutton Parlor North*
Hand Surgery/Anesthesiolgy (All Day), *Sutton Parlor South*
Urology/Dermatology, *Sutton Parlor Center*
Psychiatry (All Day), *Regent Parlor*
Realistic Uses of Computers in Medical Practice, II, *Madison Suite*
Update on AIDS, *Morgan Suite*

2:00 p.m. - 5:00 p.m.
Ophthalmology, *Beekman Parlor*
Internal Medicine, *Sutton Parlor North*
Otolaryngology, *Sutton Parlor Center*
Hand Surgery/Anesthesiology, *Sutton Parlor South*
Psychiatry, *Regent Parlor*

SUNDAY, MARCH 9

*9:00 a.m. - 1:00 p.m.
General Surgery/Colon & Rectal Surgery, *Beekman Parlor*

10:00 a.m. - 1:00 p.m.
Allergy & Immunology, *Sutton Parlor North*
Women's Medical Society of N.Y./Family Practice/Emergency Medicine, *Regent Parlor*
Pathology, *Sutton Parlor Center*

CME CREDITS: Each program will be eligible for CME Category 1 credits on an hour-for-hour basis.

Technical Exhibits

Central Park Lake

Washington Square Arch

COURTESY N.Y. CONVENTION & VISITORS BUREAU

Advance Registration Form

1986 Annual CME Assembly, March 7–9
The New York Hilton, New York City

Complete and return this form to the Medical Society address as indicated below.

Name_____
PLEASE PRINT LAST FIRST

Address_____

City/State/Zip_____

Medical Specialty_____

REGISTRATION FEE *Please check categories*

- ☐ Non-Member Physician* $50.00
- ☐ Allied Profession $10.00

* of any state medical society

- ☐ Nurse
- ☐ Physician Assist.
- ☐ Dentist
- ☐ Lab Technician
- ☐ PT/OT
- ☐ Other_____ *Specify*

NO FEE *Please check category*

- ☐ MSSNY Active Member*
- ☐ MSSNY Life Member
- ☐ Resident/Intern
- ☐ Medical Students
- ☐ Medical Assist.
- ☐ Speaker
- ☐ Spouse/Family
- ☐ News Media/Medical Writer

REMITTANCE ENCLOSED $_____

Please make check payable to:
Medical Society of the State of New York, and return this form with remittance to: Division of Meeting Services/MSSNY, 420 Lakeville Rd., P.O. Box 5404, Lake Success, N.Y. 11042.

Important: Your ID Badge will be held at the MSSNY Registration Desk located in the Exhibit Hall, on the second floor of the New York Hilton.

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MISCELLANEOUS

PROFESSIONAL CONDUCT EXPERT. Robert S. Asher, J.D., M.P.A., in health, former Director Professional Conduct, N.Y.S. Board of Regents, now in private legal practice. 15 years health law experience concentrating on professional practice, representation before government agencies on Disciplinary, Licensure, Narcotic Control, Medicaid, Medicare of Third-Party Reimbursement matters and professional business practice. Robert S. Asher, Esq., 110 E. 42nd Street, NYC. (212) 697-2950 or evenings (914) 723-0799.

ARE YOU UNDER INVESTIGATION BY THE STATE LICENSING AUTHORITIES? For consultation call Susan Kaplan, Attorney-at-Law, (212) 877-5998. Practice limited to the vital legal problems affecting your professional license with extensive trial and administrative experience—formerly Assistant Chief of Prosecution and Deputy Director of Professional Discipline (the state agency responsible for regulating NYS's 31 licensed professions), and as an Assistant District Attorney in Nassau County.

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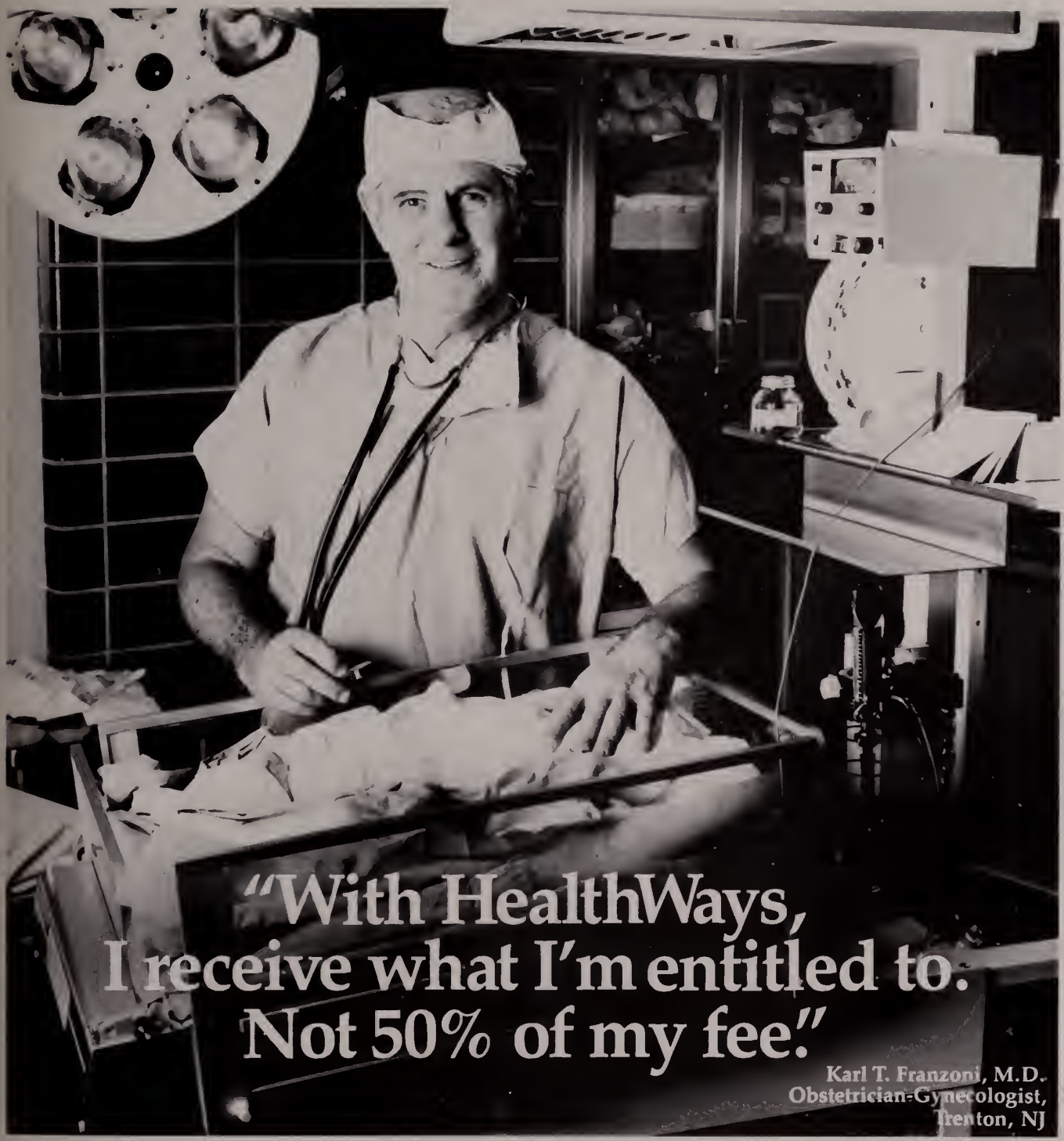

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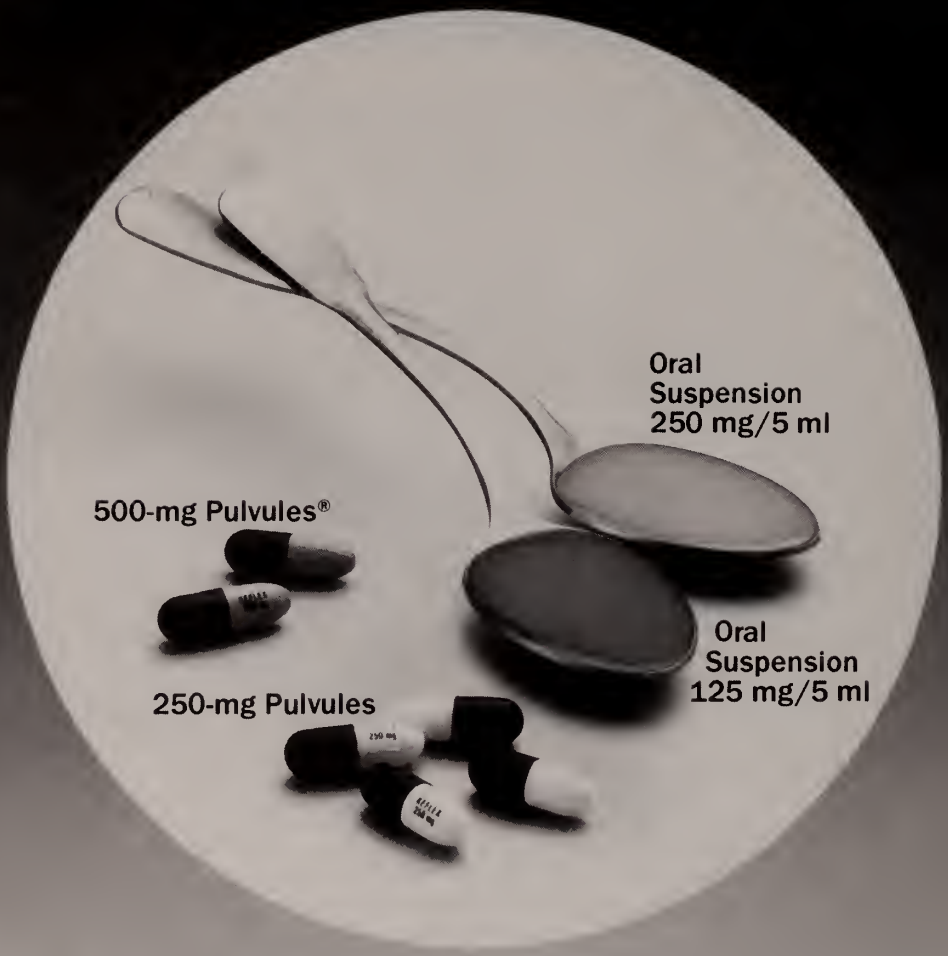

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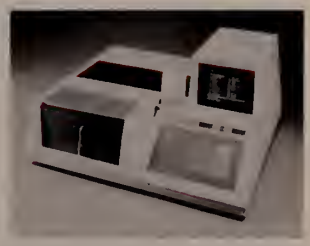

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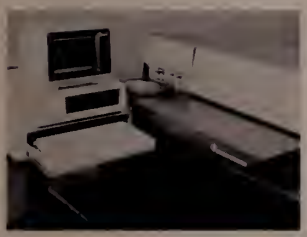

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Most adverse effects responded well to dose reduction and only rarely was verapamil discontinued. **Precautions:** ISOPTIN should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacologic effects. Studies in a small number of patients suggest that concomitant use of ISOPTIN and beta blockers may be beneficial in patients with chronic stable angina. Combined therapy can also have adverse effects on cardiac function. Therefore, until further studies are completed, ISOPTIN should be used alone, if possible. If combined therapy is used, close surveillance of vital signs and clinical status should be carried out. Combined therapy with ISOPTIN and propranolol should usually be avoided in patients with AV conduction abnormalities and/or depressed left ventricular function. 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One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. *Pregnancy Category C:* There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor and delivery only if clearly needed. It is not known whether verapamil is excreted in breast milk; therefore, nursing should be discontinued during ISOPTIN use. **Adverse Reactions:** Hypotension (2.9%), peripheral edema (1.7%), AV block: 3rd degree (0.8%), bradycardia: HR < 50/min (1.1%), CHF or pulmonary edema (0.9%), dizziness (3.6%), headache (1.8%), fatigue (1.1%), constipation (6.3%), nausea (1.6%), elevations of liver enzymes have been reported. (See *Warnings.*) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecomastia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984. 2385

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APRIL 1986

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Apr 1. **Emergency Medicine Board Review.** *Apr 10–12.* **Advances in Dermatology.** 17 Cat 1 Credits. *Apr 14–19.* **Comprehensive Review of Physical Medicine.** 57 Cat 1 Credits. *Apr 17–19.* **Speech Recognition With Cochlear Implants.** 13 Cat 1 Credits. *Apr 19.* **Breast Cancer and Mammography.** 5 Cat 1 Credits. *Apr 28–May 2.* **Interventional Neuroradiology.** 32 Cat 1 Credits. Info: NYU Medical Center Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Apr 3–4. **Gastroenterology Oncology—1986.** Info: CME Conference Planning Office, C-180, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021. Tel: (212) 794-6754.

Apr 6–9. **International Rehabilitation Week.** Jacob Javits Convention Center. Info: EJJ Management Inc., 225 West 34th St, New York, NY 10122. Tel: (212) 563-5350.

Apr 7–9. **Basic Electromyography and Electrodiagnosis.** *Apr 10–11.* **Evoked Potentials.** Info: Daoud B. Karam, MD, Rehabilitation Medicine, New York Medical College, Coler Memorial Hospital, Roosevelt Island, NY 10044. Tel: (212) 688-9400, ext. 385.

Apr 9. **How to Develop a Research Project.** Info: Beverly R. Baptiste, Medical Education, Beth Israel Medical Center, First Ave at 16th St, New York, NY 10003.

Apr 10–12. **Surgical Courses in Lens Implantation.** Info: Ruth Green, Administrator, Ophthalmological Foundation of America, 823 United Nations Pl, New York, NY 10017. Tel: (212) 986-4848.

Apr 18–19. **Laser Surgery Course.** 17 Cat 1 Credits. Info: Kristen M. Johnson, Administrator, Department of Otolaryngology, 210 East 64th St, New York, NY 10021. Tel: (212) 838-9200, ext. 2448.

Apr 19–20. **Second International Conference on Eating Disorders.** 13 Cat 1 Credits. The Waldorf-Astoria. Info: Office of Continuing Medical Education, Albert Einstein College of Medicine/Montefiore Medical Center, 3301 Bainbridge Ave, Bronx, NY 10467. Tel: (212) 920-6674.

BROOKLYN

Apr 2. **Mechanisms of Oncogene Activation.** *Apr 9.* **Perspectives on Cancer Cause and Prevention.** *Apr 23.* **Diagnosis and Treatment of Acute Non-Lymphocytic Leukemia.** Info: Division of Hematology/Oncology, Department of Medicine, Interfaith Medical Center, 555 Prospect Pl, Brooklyn, NY 11238.

Apr 17–18. **Application of the CO_2 Laser in Otolaryngology Head and Neck Surgery.** 16 Cat 1 Credits. Info: Yosef P. Krespi, MD, Robert K. Einhorn, MD, Long Island College Hospital, Department of Otolaryngology, Room 460, Brooklyn, NY 11201. Tel: (718) 780-1281.

NASSAU

Apr 8. **Neutropenic Patient.** 1 Cat 1 Credit. *Apr 29.* **Adverse Drug Reactions—Practical Aspects.** 1 Cat 1 Credit. Info: The Community Hospital at Glen Cove, St. Andrews La, Glen Cove, NY 11542. Tel: (516) 676-5000.

Apr 9. **Coronary Artery Disease: Medical Versus Surgical Therapy.** *Apr 23.* **Frontiers in Cardiac Imaging: Digital Subtraction Angiography.** Info: Medical Education Department, Mercy Hospital, 1000 North Village Ave, Rockville Centre, NY 11570. Tel: (516) 255-2260.

Apr 18. **Continuing Topics in Neurology.** 6 Cat 1 Credits. Info: Bernard W. Berkowitz, MD, Department of Neurology, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-3107.

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(*Continued on p 13A*)

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References:
1. Strauss WE, McIntyre KM, Parisi AF, et al: Safety and efficacy of diltiazem hydrochloride for the treatment of stable angina pectoris: Report of a cooperative clinical trial. Am J Cardiol 49:560-566, 1982.
2. Pool PE, Seagren SC, Bonanno JA, et al: The treatment of exercise-inducible chronic stable angina with diltiazem: Effect on treadmill exercise. Chest 78 (July suppl):234-238, 1980.

Reduces angina attack frequency*
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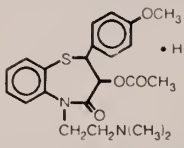
2/84

PROFESSIONAL USE INFORMATION

DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy)-5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+)-cis-. The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina. CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given, a 120-mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy**—CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

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COMMENTARIES

A perspective on the heterosexual transmission of the acquired immunodeficiency syndrome

An important question facing epidemiologists studying the problem of the acquired immunodeficiency syndrome (AIDS) in the United States is why it continues to appear primarily in the homosexual and intravenous drug abusing populations. Indeed, up until this point, heterosexuals account for only 1% of all US AIDS cases, and have throughout the history of the epidemic.[1] This is reinforced by the low prevalence of HTLV-III/LAV seropositivity in the heterosexual community. Serologic screening among volunteer blood donors in the United States has shown that only approximately 0.04% of that population have antibodies to HTLV-III/LAV. Indeed, retrospective questioning of 35 of 41 such individuals who did have confirmed serum antibody demonstrated that they belonged to high risk groups for AIDS.[2]

However, the epidemiology of the disease in certain regions in the developing world suggests that heterosexual activity may be a major mode of transmission of the AIDS virus. In Zaire, the ratio of men to women with the disease is 1.1:1,[3] and in both Rwanda[4] and Haiti,[5] heterosexual promiscuity appears to be a risk factor for AIDS among both men and women. An equal seroprevalence of roughly 60% for antibodies to HTLV-III/LAV among both the male sexual partners of female AIDS patients and female sexual partners of male AIDS patients in Haiti is further evidence of bidirectional heterosexual transmission in the developing world.[6] Although US studies of female sexual partners of intravenous drug abusers[7] and female sexual partners of hemophiliacs[8] have provided strong evidence that the virus may be transmitted from men to women via sexual intercourse, firm epidemiologic evidence does not yet exist that the AIDS virus is being transmitted from women to men in the western world. The lack of such evidence for female-to-male spread in the United States may account for the absence of extensive heterosexual spread in this country and provide important clues for reducing risk. One could envision a scenario in the developed world in which male-to-female transmission would occur with relative efficiency, but female-to-male transmission would be far less likely. In this setting the chain of transmission allowing extensive spread of disease into the heterosexual population would be broken.

If heterosexual activity is responsible for the bidirectional transmission of HTLV-III/LAV in the third world, then some aspect of sexual activity in the less developed countries may be important in enhancing transmission. Other sexually transmitted diseases may be such a factor. These infections provoke a lymphocyte response that may increase the ease of virus inoculation from an HTLV-III/LAV infected individual. In addition, these sexually transmitted diseases may disrupt the integrity of the mucosa or skin, allowing invasion of HTLV-III/LAV into the new hosts. It is known that receptors for HTLV-III/LAV are present on subsets of T-lymphocytes and perhaps certain cells of the central nervous system, but it is not likely that receptor-bearing cells are exposed on the intact male genitalia. Therefore, in the absence of a lesion or chancre, even when the penis is inserted into an infected orifice, infection may not occur.[9] Sexually transmitted diseases are widespread both in Africa[10] and Haiti,[5] and may provide an explanation for the apparent bidirectional transmission of this virus in those regions. In the western world, where venereal disease rates are lower, female-to-male transmission could well be less likely.

The association of sexually transmitted diseases and AIDS in third world countries is perhaps confounded by the practice of the frequent reuse of unsterilized needles and syringes. In Haiti, for example, nonmedical practitioners called *piquristes* often give injections of antibiotics or vitamins to patients with needles that have not been sterilized (personal observation). One could speculate that individuals with a history of sexual promiscuity would be more likely to acquire sexually transmitted diseases and then receive injections from these *piquristes* as therapy for their symptoms and acquire HTLV-III/LAV infection from contaminated needles or syringes. While this

phenomenon deserves more attention, it is unlikely that heterosexual transmission of such apparent magnitude as occurs in the third world can be entirely explained by this practice.

In summary it appears possible that the biological setting for heterosexual activity in the developed and the developing worlds may differ in ways that may influence the likelihood of bidirectional transmission. Of course the alternative exists that this disease has so far confined itself largely to the homosexual population but given time will spread among heterosexuals. However, it seems just as likely that a nationwide epidemic of the magnitude that has been observed in the homosexual and intravenous drug abusing populations will not occur in the heterosexual population in the developed world.

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The epidemiology of the acquired immunodeficiency syndrome in Africa

The problem of the acquired immunodeficiency syndrome (AIDS) in sub-Sahara Africa has attracted the attention of medical scientists and the general public in the developed world, not least of all because preliminary epidemiologic data indicate a pattern of heterosexual transmission.[1] Yet AIDS in the two areas of the world where its epidemiology has been carefully studied, the United States and western Europe, is clearly a disease whose transmission is overwhelmingly associated with homosexual activity and the use of unsterile needles and syringes.[2] In the developed world, the users of the latter are primarily intravenous drug abusers. However, in the developing world, and in sub-Sahara Africa in particular, unsterile reused needles and syringes are widely employed for reasons that will be elaborated.

If indeed AIDS is primarily transmitted heterosexually in Africa, as may be inferred from the currently available data, then theoretically such a mode of transmission could become established in western Europe and the United States. The implications of this are far reaching and of great concern. Gay groups in the United States who lobby for increased funding for AIDS research understandably muster this evidence in a selective manner in order to draw on the strength of a potentially larger constituency. Yet in the several years since AIDS has been carefully monitored in the United States, there are no data to support the contention that heterosexual transmission is epidemiologically significant. It should be noted parenthetically that the feasibility of both male-female and female-male transmission of HTLV-III/LAV, the virus responsible for both AIDS and AIDS-related complex (ARC), has been demonstrated.[3,4] These studies were conducted by Redfield and coworkers among Army personnel, some of whose only alleged risk factors were promiscuous heterosexual activity or contact with prostitutes. Critics have pointed out, however, that these studies among Army personnel and their spouses must be interpreted with considerable caution.[5] An admission of drug abuse or homosexual activity by US military personnel results in automatic discharge. Thus the reported heterosexual promiscuity and its association with AIDS might be coincidental and not causal in some individuals who also are drug abusers or who engage in homosexual activity and who hide these facts out of fear of discharge.

The studies by Redfield and coworkers demonstrate that heterosexual promiscuity was a prominent feature in 13 of 17 individuals who acquired HTLV-III/LAV disease. Eight of these patients admitted to contact with

more than 50 partners and five to contact with more than 100 partners over the previous five years.[4] This finding, if not confounded by the variables mentioned above—drug abuse or homosexual activity—identifies a common denominator with many documented cases in Africa, namely promiscuity, that is also a prominent feature of cases among homosexuals in the United States and in Europe.

The existence of AIDS in Africa was first uncovered by physicians in both Brussels and Paris in 1983 who treated patients from Africa for a disease identical to that seen in homosexuals, drug abusers, and the recipients of blood products in the United States.[6,7] Laboratory studies later confirmed that it was indeed the same disease,[8] and eventually in 1984 the results of field studies in both Rwanda and Zaire confirmed the existence of both the clinical disease and its immunologic features.[1,9] Since these early reports, a great deal of information has accumulated about the clinical features of AIDS in Africa. There are distinct differences in the opportunistic infections that affect African patients with AIDS; candidiasis, tuberculosis, cryptococcal meningitis and sepsis, cryptosporidiosis, herpes simplex, and cytomegalovirus choreoretinitis.[10] Whereas *Pneumocystis carinii* pneumonia is found in almost one half of AIDS patients in Europe and the United States, it is infrequently found in African patients with AIDS in Europe.[10] Biggar concluded that the rapid progression of *P. carinii* disease might limit the number of patients with it who make it to Europe for treatment.[11] Clearly, the opportunistic infections seen in African patients with AIDS both in Africa and Europe reflect the pathogens to which they are exposed. The benign form of Kaposi's sarcoma has long been observed in Africa as well as in developed countries.[12] Recently, however, the aggressive form of Kaposi's sarcoma has been well documented in areas such as Zambia where a high prevalence of AIDS has been found.[13]

The available evidence points to the fact that AIDS as we now know it is a relatively new disease in sub-Sahara Africa (personal observations, personal communications). This is also supported by the fact that affluent Africans evacuated to European hospitals for complex medical problems were not observed to have the disease prior to 1980.[14] Not surprisingly it has been found that AIDS in Africans seen in Europe occurs among the economically and socially affluent classes.[8] It would be inaccurate to assume that these patients reflect the actual social distribution of the disease in Africa. In epidemiologic terms, these patients represent that subset of cases who because of wealth and political status have ready access to tertiary care in Africa, where the diagnosis is likely to be made, and to medical evacuation to Europe at government expense. In French speaking countries of Africa, a significant portion of the annual budgets of ministries of health are set aside for the medical evacuation of patients to Europe and for care received there. In Mali during the 1970s upwards of 10% of the health budget was so allocated (personal observation). Thus one cannot draw any meaningful epidemiological conclusions about the general incidence of a disease in Africa solely based on cases seen among patients evacuated to Europe. Likewise, data based on cases seen in large city hospitals may also be misleading. These cases represent that segment of society with either geographic, social, or economic access to large tertiary care facilities whose medical staffs are more likely to recognize the disease. These observations in large city hospitals accumulate data through passive surveillance (case detection among those presenting for treatment). They cannot really tell us what is happening in the population at large with either AIDS or any other disease. Indeed data are now accumulating that AIDS is, as one might have suspected all along, distributed among rural populations as well.[15]

It is important to remember that in sub-Sahara Africa, class formation of the type common in developed countries is a recent phenomenon. Social mobility characterizes much of the population. Even the new affluent elite have constant contacts with their extended families and those from the same region of origin. There is enormous physical mobility to and from the cities, which is often seasonal in nature.[16] There is also a wide range of regional movements based on trade and commerce. Thus the frontiers between classes and between the cities and the bush are open ones. On this basis alone it is difficult to conceive of AIDS as being confined to affluents living in the cities. Rather it is these persons who come to medical attention and their disease diagnosed while the poorer rural population may not even seek medical care at a modern medical care facility. Most rural Africans, and a significant number of Africans living in cities, consult traditional healers sometimes but not always to the exclusion of modern medical care practitioners.[17,18] This can have an enormous effect on prevalence data gathered through passive surveillance.

The imperfect epidemiologic data gathered in Africa point to a heterosexual distribution for AIDS. These data, such as those gathered in Rwanda and Zaire, show an almost 1.1:1 male to female ratio, compared to the 19:1 male to female ratio in the United States and Europe.[8,9] Most cases reported are in those age groups for which sexual activity is greatest. Yet cases are being reported now among children as well.[19]

The passive surveillance data point to heterosexual promiscuity as being an important risk factor in the transmission of AIDS. Homosexual activity and drug abuse are vehemently denied by Africans (personal observation). However, the former, while rare, is not unknown and the latter is much more common than African health officials are willing to admit. Yet it appears that homosexual and bisexual activity and intravenous drug abuse play a small role in the disease's transmission in Africa. Similarly sexual practices among heterosexual partners such as anal intercourse and orogenital contact are virtually unknown in most African societies. Thus it is unlikely that they constitute risk factors for AIDS transmission as they do in the United States and in Europe.

The hypothesis that the use of improperly sterilized needles and syringes contributes to the spread of AIDS in Africa deserves serious attention. The use of improperly sterilized, reused injection equipment in sub-Sahara Africa is widespread. It is so widespread in fact as to potentially confound whatever epidemiologic data are generated through either passive surveillance (case detection among those presenting for treatment) or active surveillance (detecting cases through systematic examination of popula-

tion groups). This mode of transmission has been discounted by some because so many of the known cases to date occur among those in the sexually active age groups. The absence of pediatric cases, so the argument goes, speaks against parenteral transmissions via dirty needles and syringes, as well as against insect transmission. Yet the epidemiologic data base is imperfect at present, and it would be unwise to categorically dismiss parenteral transmission. Even if it is not significant at present, parenteral transmission may assume significance in the future for a variety of interrelated reasons.

In many areas of sub-Sahara Africa there exists a cultural preference for medications delivered by injection. This preference often has its roots in traditional beliefs about disease causation and how these causes may be neutralized.[20] The colonial medical services, which introduced needles and syringes, provided suitable substitutes for scarification linked to cupping and the application of herbal salves and poultices to the external areas of the body. Colonial medical authorities consistently reinforced the preference for injectable medications out of a desire to achieve compliance. It was observed then, as now, that pills were often not taken, taken improperly, given away as gifts, sold, or simply thrown away. The confluence of these two historic variables led to the widespread belief in the greater efficacy of injectable medication over pills and tablets.

In the former French colonies in sub-Sahara Africa, French medical prescribing practices were effectively transferred to both African physicians and to patients. These prescribing practices are characterized by long lists of medications, many of them nonspecific, for the treatment of any given disease. Thus a patient with a presumed bacterial infection will be given a prescription for several antibiotics (most to be administered by injection), injectable vitamins and minerals, and injectable stimulants. The prescription does not constitute a legal document, but simply a convenient shopping list as most drugs, when available, are sold over the counter. Patients expect the prescription to contain a long list of drugs and are dissatisfied if this expectation is not met.

The next step for the patient is to have the medications administered. If they are hospitalized this is done by the hospital staff, but they often must still obtain the drugs. An outpatient most often does not return to the physician for the injections. Rather he or she has them administered by someone in their neighborhood who possesses both the needles and syringes and the knowledge for using them. These individuals are often nurses, of varying levels of training, who make a substantial side income by giving injections. These persons are often employed in government dispensaries, hospitals, and clinics, and they provide significant levels of primary care. Their numbers are currently considerable because African countries opted at independence in the early 1960s to train quickly large numbers of paramedical personnel to meet urgent medical manpower needs.

Very often the needles and syringes used by these personnel both in their places of employment and their "private injection practices" are supposedly "sterilized" by being dipped in rubbing alcohol. The needles are often meticulously swabbed with cotton saturated with rubbing alcohol just prior to injection. In large dispensaries, needles are frequently "sterilized" by being placed in a shallow pan to which rubbing alcohol is added in small amounts. A lighted match is then thrown in and the needles shaken about. Clearly all of these means of "sterilizing" needles and syringes are inadequate. Not infrequently needles and syringes used in dispensaries, clinics, and hospitals are either not sterilized or inadequately boiled or autoclaved.

The ranks of paramedical personnel giving injections have grown by the addition of traditional medical practitioners who in some countries have achieved quasi official recognition. This has come about in part because of incentives to integrate traditional medicine and the modern medical care system. Many traditional practitioners have shown a remarkable ability to absorb the accoutrements of modern medicine by wearing white coats, calling themselves "doctor," and using needles and syringes to give modern medications. Most of these individuals are completely lacking in knowledge of the microbial causes of communicable diseases and of the need to sterilize needles and syringes.

Given the widespread presence of the HTLV-III/LAV agent in Africa, the current preferences for injectable medications, the widespread reuse of improperly sterilized needles and syringes, and the financial incentives for paramedical personnel and others to continue giving injections, it is unlikely that parenteral transmission will not assume some importance if it has not already done so.

Polk has pointed out that the bidirectional heterosexual transmission pattern seen in Africa may be confounded by the medical reuse of inadequately sterilized needles and syringes.[5] The fact that prostitutes in some urban areas of Africa show a high incidence of the disease may not necessarily be reflective of promiscuity linked to heterosexual activity. Rather as individuals subjected to repeated bouts of sexually transmitted diseases, causally associated with heterosexual promiscuity, they are more likely than most to be exposed to the risk of contaminated injection equipment while undergoing treatment for these diseases.

There is one important caveat about equating the reuse of unsterile needles and syringes in Africa with their reuse among intravenous drug abusers in the US and western Europe. Among the latter, drugs are often administered in a group setting, with the injection equipment being passed around from one person to another. This practice plus injection techniques used by addicts maximizes the risk of passage of fresh body fluids, blood, and serum as well as viral agents such as HTLV-III/LAV from one person to another. In sub-Sahara Africa the reuse of unsterile injection equipment may not be immediate. Minutes, hours, and even days may elapse before reuse. Such temporal factors in concert with physical environmental conditions may affect the viability of the HTLV-III/LAV virus. Thus projections concerning the transmission of AIDS through unsterile needles and syringes in Africa would have to be based in part on a consideration of the extracorporeal viability of the virus and of those factors that affect it.

The epidemiology of AIDS in sub-Sahara Africa is incompletely understood at present. The current observation that the disease is primarily found in sexually active heterosexual adults does not mean that such a distribution

will eventually be found in the US and Europe. For if this observation is an accurate epidemiologic profile of the disease in Africa, and it might well be, there may be cofactors such as concurrent sexually transmitted diseases and previous assaults with numerous infectious agents that may enhance the likelihood of infection with HTLV-III/LAV in Africans.

There are confounding variables that must be evaluated in studying the epidemiology of AIDS in Africa. Sorting these out in well-designed epidemiologic studies will not be an easy matter. Until extensive valid data based on such studies are generated it would be inappropriate to come to definitive conclusions about the epidemiology of the disease in Africa. Likewise it would be unwise to use current preliminary epidemiologic observations in Africa as a basis for extrapolating predictions about the future pattern of transmission of AIDS in Europe and in the United States.

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Heroin addiction: insights from Alexis de Tocqueville

In his article, "Heroin and Medical Reasoning: The Power of Analogy," in this issue of the Journal, Gregory J. Higby of the University of Wisconsin, Madison School of Pharmacy, chronicles the brief but validly therapeutic use of heroin, first for specific respiratory illnesses, then to relieve pain, and its final rejection by the medical profession as its addictive properties were realized. The euphoria produced by heroin came to be, for its users, its most important effect.[1] This latter use of heroin reflects the surprising number of descriptions of the American character suggesting the desire or need to "feel better" or "get high." Alexis de Tocqueville observed in his *Democracy in America* that the "dominant passion" among the citizens of the new society he visited was the desire to acquire "the good things of this world."[2] However, he wrote, this concentrated search for material possessions eventually took its toll, for the soul needed satisfaction that material distractions could not provide.

> If their social condition, circumstances, and laws did not so closely confine the American mind to search for physical comfort, it may well be that when they came to consider immaterial things they would show more experience and reserve and be able to keep themselves in check without difficulty. But they feel imprisoned within limits from which they are apparently not allowed to escape. Once they have broken through these limits, their minds do not know where to settle down, and they often rush without stopping far beyond the bounds of common sense.[2]

Although de Tocqueville recognized that this spectacle of restlessness in the midst of abundance was "as old as the world," he was astonished at its pervasiveness among the people of this new democracy.[2] The leveling of society resulted in an insatiable need that "every instant [Americans] think they will catch ... and each time it slips through their fingers." From these symptoms de Tocqueville derived a "strange melancholy often haunting inhabitants of democracies in the midst of abundance, and of that disgust with life sometimes gripping them in calm and easy circumstances."[2]

Although de Tocqueville did not intend for his comments to apply to substance abuse, his observations are nonetheless as relevant today as they were at the time of his visit more than 150 years ago. At that time religious ecstasy filled the emptiness of those whose aspirations were "closed in by the wretchedness of the actual world"[2];

the 20th century has its counterpart in substance abuse.

When looking at America's tragic encounter with heroin addiction, it is difficult to separate the causes from those observations made by de Tocqueville, or from the causes that applied to earlier substance abuse. Opophagia—opium eating—was the secret scourge of Victorian society, initially among the veterans of the Civil War and later among white middle-class women. In the 20th century, heroin became the solace for a new generation of substance users, principally certain minority communities in America. Despite this transference of race and class, the causes are surprisingly Tocquevillean. Faced with the eschatological promises of a democratically just society, certain minorities found themselves closed off by the squalor of poverty, inequality, injustice, and alienation. Substance addiction became a calming and easy escape.

For too long, heroin abuse remained a ghetto problem, remote from the eyes and ears of white upper- and middle-class America. The use of mind-bending substances by Victorian women at the beginning of the century, habituated by therapeutic prescriptions, was considered an indication of woman's frailty and as such a problem of gender, not of society. As Higby notes in his article, physicians considered those patients who became addicted to medically prescribed heroin to be constitutionally susceptible or weak. The movement of heroin use into communities other than skid rows, tenderloin districts, or racially segregated areas was a slow snowball gathering speed. Only when drug abuse moved into the headlines and into white communities like Haight-Ashbury, San Francisco, home of the flower children of the 1960s, and when it affected returning Vietnam veterans, did the broader culture become reluctantly aware of its pervasiveness. Among the stresses of modern society, and the need for instant solutions to all problems (along with instant coffee and computer-speed analysis) the use of heroin and other chemical substances to produce escape or euphoria have been a part of the mainstream American middle class of today that needs, as did the society de Tocqueville observed, satisfactions of the cravings of mind and soul. Today, chemical descendants of heroin have made inroads into every recess of American life and the spectre of Huxley's *Brave New World* of somma pills becomes more of a reality.

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1. Higby GJ: Heroin and medical reasoning: the power of analogy. *NY State J Med* 1986; 86:137–140.
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NEW EDITOR OF THE *JOURNAL*

Pascal James Imperato, MD, has succeeded Alan Blum, MD, as Editor of the *New York State Journal of Medicine* effective January 1, 1986. He joined the editorial staff of the *Journal* in 1983 as consulting editor and later became deputy editor and book review editor. Dr Imperato received his MD degree from the State University of New York, Downstate Medical Center in 1962. While a student there he was awarded a foreign fellowship by the Association of American Medical Colleges and the Smith, Kline and French Laboratories in order to study tropical diseases in Kenya and Tanzania, where he spent much of his fourth year. He completed his internship and residency in internal medicine at Long Island College Hospital in New York City after which he was awarded the New York Academy of Medicine's Glorney-Raisbeck Fellowship in the Medical Sciences for one year of study at Tulane University's School of Public Health and Tropical Medicine from where he received an MPH & TM degree. Part of this year was spent at Tulane's International Center for Medical Research and Training in Cali, Colombia.

From 1966 to 1972 Dr Imperato was a medical epidemiologist with the Center for Disease Control, USPHS, assigned to the West African country of Mali. There he directed a smallpox eradication and measles control program and initiated efforts to control epidemic meningococcal meningitis, cholera, and yellow fever. He also served as a technical advisor on mobile medical services to the ministries of health of several West African countries. In 1971 he was awarded the Meritorious Honor Award and Medal of the US Department of State for his work in Africa. During the 1970s he made several return visits to both West and East Africa, primarily as a consultant for the US Agency for International Development.

Beginning in 1972, Dr Imperato successively served in the New York City Department of Health as Director of the Bureau of Infectious Disease Control and First Deputy Commissioner, being appointed Commissioner of Health and Acting Health Services Administrator in 1977. He also served as Chairman of the Board of the New York City Health and Hospitals Corporation, the New York City Board of Health, and the Executive Committee of the New York City Health Systems Agency. In 1972 he joined the faculty of Cornell University Medical College in both the departments of public health and medicine and became an assistant attending physician in medicine at New York Hospital.

Since 1978 Dr Imperato has been professor and chairman of the Department of Preventive Medicine and Community Health, State University of New York, Downstate Medical Center and adjunct professor of Public Health at Cornell University Medical College. In 1984 he was named a Senior Fulbright Fellow. Dr Imperato has authored more than 100 articles in peer-reviewed medical and scientific journals and 15 books, a number of which deal with Africa. His most recent works are *The Administration of a Public Health Agency* (1983) and *Acceptable Risks* (1985), published by Viking Press. The latter book, which deals with health risks in modern society, such as poor dietary habits, environmental hazards, dangerous lifestyles, cigarette smoking, and other issues, has received widespread national recognition.

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Clinical assessment of metabolic bone disease

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ABSTRACT. Twenty-one patients with atypical metabolic bone disease were evaluated by biochemical parameters and by iliac crest bone biopsy using a simplified method of quantitative bone histomorphometry. These patients were uncommon in that their disease was often quite severe and of either unknown cause or due to many factors. Biopsy specimens were studied in a way that could be performed in most hospital settings. Patients ranged in age from 27 to 84 years and many had risk factors for osteopenia, such as gastrointestinal disorder, prior gastric surgery, use of corticosteroids or anticonvulsants, poor nutrition, and early menopause. Bone biopsy results were correlated with a variety of clinical and laboratory data, including a calcium loading test. These initial correlations might aid in understanding the factors involved in the pathogenesis of bone disease in general and set the groundwork for future prospective confirmatory studies. The predictive value of clinical laboratory data was also explored in terms of bone biopsy findings. The most common biochemical abnormality found was a decreased serum albumin (15 of 21, or 71%). Fasting hypercalciuria was present in seven of 17 (41%). There was a positive correlation between the 25-hydroxyvitamin D level and the increase in urinary calcium after an oral calcium load. Of 21 patients 17 (81%) had decreased trabecular bone volume. None of the patients had an increase in trabecular osteoid volume sufficient to make a diagnosis of osteomalacia, although several had increased trabecular osteoid surface suggesting an increase in bone turnover. Parathyroid hormone (PTH) levels were within the normal range but still correlated inversely with trabecular bone volume, suggesting PTH involvement in the production of decreased bone mass. Serum albumin correlated inversely with the trabecular osteoid surface. The results of this study suggest several mechanisms in the production of metabolic bone disease. They also suggest that clinical laboratory data are often insufficient for the differential diagnosis of osteopenia. Bone biopsy with double tetracycline labeling and quantitative histomorphometric analysis will still provide the best means of diagnosis.

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Differential diagnosis of metabolic bone disease is an increasingly frequent clinical problem, not only because the population is aging, but because clinicians have become more alert to the existence of this disorder.[1] Patients who present with the vertebral crush fracture syndrome, fractures with minimal trauma, or decreased bone mass on routine radiologic examination are difficult to evaluate. The diagnosis is frequently based on exclusion and probabilities. For example, a postmenopausal woman who does not have any evidence of malignancy, thyrotoxicosis, or primary hyperparathyroidism is usually presumed to have osteoporosis, a syndrome characterized by decreased bone mass with normal mineralization. However, some of these patients will show impaired mineralization (osteomalacia) as well. The combination of osteoporosis and osteomalacia may be particularly frequent in elderly individuals who have some abnormality that is likely to lead to a decreased supply of calcium or phosphate, such as gastrointestinal or renal disease, impaired dietary intake of vitamin D, or decreased exposure to sunlight.[2–8] When the patient is not a postmenopausal woman, the differential diagnosis becomes even more critical because the likelihood of osteoporosis decreases as compared with other disorders.

A complete work-up for various causes of osteopenia is expensive and difficult to assess. Ultimately, unless a specific causative factor is identified, the only procedure that will differentiate osteomalacia and osteoporosis and can help assess the degree of osteopenia is a bone biopsy. However, an ideal bone biopsy requires the use of a large nee-

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dle that will provide a sample of relatively intact bone that has not been crushed or distorted, the preparation of an undecalcified section that requires a special microtome, and fluorescence labeling with tetracycline to determine whether the new osteoid is being mineralized normally. In most published studies the biopsy specimens are subjected to extensive quantitative histomorphometric analysis that is time consuming and requires considerable training.[9]

This report concerns the clinical evaluation of 21 patients referred for symptomatic disease. These patients were uncommon; their disease was often quite severe and of either unclear cause or was caused by many factors. Bone biopsies and calcium loading tests were performed in an attempt to define the disorder in terms of pathogenesis. Calcium-loading tests have been used in the past largely to assess patients with hypercalciuria in whom increased intestinal calcium absorption may be detected by an increased excretion of an oral calcium load.[10,11] It was questioned whether impaired absorption could be tested in the same manner. Biopsies were initially given a subjective nonquantitative pathologic diagnosis. The histomorphometric evaluation of bone biopsy specimens as commonly performed in clinical research is too cumbersome and time consuming for routine clinical practice. In this study, biopsy specimens were examined in a way that could conceivably be carried out in most hospital settings.

The predictive value of clinical laboratory data in terms of bone biopsy findings was also considered. After the data were obtained on this group of patients, they were screened for correlations that might aid in understanding the factors involved in pathogenesis of bone disease in general. This information would help set the groundwork for possible future prospective studies testing the significance of the findings.

TABLE I. Biochemical Data of Study Group

No	Age/Sex	Symptoms	Associated conditions	Fractures	Clinical diagnosis	Pathologic diagnosis
1	69/F	Low back pain	—	Dorsal compression	Osteoporosis	Osteoporosis; mild osteomalacia
2	76/F	Back pain	Status post gastrectomy, history of temporal arteritis and steroid use	Vertebral wedging	Osteoporosis	Osteoporosis; osteomalacia
3	60/F	Back pain	Estrogen replacement	Dorsal compression	Osteoporosis	Osteoporosis
4	69/M	Low back pain	Asthmatic bronchitis, on steroids, history of partial gastrectomy	Sacral vertebrae	Osteoporosis	Osteoporosis; mild osteomalacia resorption
5	70/M	Low back pain	Chronic lymphocytic leukemia, diabetes	Compression L2, L3, L4	Osteopenia	Osteoporosis; mild osteomalacia
6	57/F	Back pain	Depression,-menopause at age 39	Compression L1	Osteopenia	Osteoporosis
7	31/M	Back pain	Renal calculi	Lumbar compression	Osteopenia	Osteoporosis
8	62/F	Back pain	Hepatomegaly, jaundice	Dorsal and lumbar compression	Osteoporosis	Osteoporosis; resorption
9	70/M	Low back pain	Rheumatoid arthritis, history of steroid use, on Vit D	Compression T11, T12, L3	Osteoporosis	Osteoporosis; mild osteomalacia
10	54/F	Muscle cramps and spasm	Nontropical sprue, malabsorption	Wedging of T11	Osteopenia	Osteoporosis; osteomalacia
11	44/F	Low back pain	Obesity, amenorrhea, anosmia	Wrist	Osteopenia	Osteoporosis
12	29/M	Low back pain	Schizophrenia, institutionalized	Compression T2–T8	Osteomalacia	Osteoporosis; osteomalacia
13	54/F	—	Hysterectomy, oophorectomy, thyroidectomy (thyroid cancer), seizures (on Dilantin)	Femur, ankle, wrist	Osteopenia	Osteoporosis; osteomalacia
14	27/F	—	Anorexia nervosa, on replacement steroids for questionable adrenal insufficiency	—	Osteopenia	Osteoporosis
15	62/F	Shoulder pain	—	—	Osteopenia	Osteoporosis
16	69/F	Diffuse bone pain	Status post vagotomy and pyloroplasty (PUD), history of estrogens, on Vit D	Compression T11, ribs	Osteopenia	Osteoporosis
17	42/F	—	Anorexia nervosa	Pelvis, tibia, fibula, ribs	Osteopenia	Osteoporosis; osteomalacia
18	51/F	Diffuse bone pain	Obesity, status post intestinal bypass, rheumatic heart disease	Ribs, femoral neck	Osteopenia	Osteoporosis; mild osteomalacia resorption
19	54/M	Low back pain	Mild diabetes mellitus, alcohol abuse, osteoarthritis	Compression L1, L2, L3	Osteopenia	Osteoporosis
20	84/F	Low back pain	Osteoarthritis, hip prosthesis, early menopause (age 38), on Vit D	Compression T11, L5	Osteoporosis	Osteoporosis
21	36/F	Joint pain	Juvenile rheumatoid arthritis, peptic ulcer disease, history of steroids (age 3–9 yrs)	—	Osteopenia	Osteoporosis

Patients and Methods

Twenty-one of the more than 40 patients who underwent biopsies between 1977 and 1980 were selected for study on the following basis: 1) the metabolic bone disease was not typical and readily diagnosed clinically; 2) adequate biochemical data were available (Table I); 3) a clear cut diagnosis of osteomalacia could not be made from these clinical or chemical data; and 4) the patients had clinical evidence of osteopenia. Fourteen of 21 patients had vertebral compression fractures and four had fractures of the appendicular skeleton. The remaining three showed radiologic osteopenia without fractures.

Laboratory studies included calcium, phosphorus, albumin, creatinine, alkaline phosphatase, immunoreactive parathyroid hormone (PTH) (C-terminal assay, Nichols Laboratory), 25-hydroxyvitamin D, and serum protein electrophoresis. Thyroid function studies were performed in most patients. Calcium loading tests were performed in 17 patients by a modification of the method of Pak.[10] The patients were kept on a modified calcium-restricted diet (avoidance of foods with high calcium content) for at least three days. A fasting two-hour urine and a four-hour urine obtained after an oral load of 1 g of elemental calcium were assayed for calcium, phosphorus, hydroxyproline (in preload specimen only), cyclic adenosine monophosphate (AMP), and creatinine. These values, as well as calculated data relating the results to creatinine excretion, were correlated with each other and with various parameters of the bone biopsy.

Transilial biopsies were performed under local anesthesia using a 6 mm Bordier trephine. Undecalcified sections were fixed in ethanol, dehydrated, cut on a Jung microtome, and stained with Goldner's trichrome stain. One to two 100 μm thick stained sections were analyzed from each case.

The biopsy specimens were qualitatively inspected and then analyzed quantitatively by using methods of point and intersection counting.[12] Measurements were facilitated by superimposing a test grid consisting of 100 points and ten semicircular lines on a light microscope projection screen.[13] For each case, 30 fields were measured which corresponds to a total number of 3,000 test points applied. This number was determined by calculating the accumulated standard deviation of increasing numbers of fields for the smallest volume fraction, osteoid. The standard deviations of osteoid volume and surface density appeared to level off between 25 and 35 fields. All measurements are carried out at 400× magnification.

The following static parameters are quantitated.[14,15] 1) Trabecular bone volume (TBV): the percent of intercortical iliac bone area that is trabecular bone (calcified tissue + osteoid). 2) Trabecular osteoid surface (TOS): percent of the total trabecular surface covered with osteoid. 3) Trabecular osteoid volume (TOV): relative osteoid volume expressed as percent of trabecular bone that is osteoid.

Results

The results of the biochemical studies appear in Table II. The most common abnormality found was a decreased serum albumin that was present in 15 patients. Largely because of this, total serum calcium was decreased in four patients. However, in only one patient (No. 10) was serum calcium concentration low when corrected for the low albumin. Alkaline phosphatase was definitely elevated in seven of 18 patients. Both immunoreactive PTH and 25-hydroxyvitamin D levels were in the normal range but varied widely. Only one patient showed an abnormal urinary cyclic AMP (No. 4). This patient also had an elevated alkaline phosphatase and was considered to be at risk for osteomalacia because of glucocorticoid treatment and a partial gastrectomy. One patient with a history of renal calculi had an elevated urinary hydroxyproline (No. 7), but otherwise normal values. Of the other patients with elevated alkaline phosphatase, one had hepatic disease (No. 8) while two others had diabetes mellitus (Nos. 5,19). It is not known whether diabetes played a role in the enzyme abnormality. Fasting urine calcium excretion and the response to an oral calcium load varied widely. Seven of 17 patients had fasting hypercalciuria. The one patient (No. 6) with marked fasting hypercalciuria and a marked response to an oral calcium load had a borderline elevated 25-hydroxyvitamin D level. No other explanations for the degree of hypercalciuria could be found. Although the 25-hydroxyvitamin D levels were generally within the normal range, there was a positive correlation between the absolute level and the increase in urinary calcium that occurred after a calcium load ($R = .80$, $P < .01$) (Fig 1, lower right). Immunoreactive PTH and urinary cyclic AMP showed a reasonably close positive correlation ($R = .62$, $P < .04$) (Fig 1, upper right) suggesting that

TABLE II. Laboratory Data

No	Ca	P	Alb	CCr	PTH	Alk Phos	25-OH D	cAMP	Ca/Cr*	ΔCa/Cr*	Hyp/Cr
1	4.5	3.7	3.6	82	80	90 (1)	80	3.4	167	269	10.2
2	4.3	4.3	3.1	115	61	83 (1)	26	3.5	340	−14	21.5
3	4.5	4.4	3.5	66	—	60 (1)	16	2.3	57	93	9.2
4	4.5	4.1	3.6	36	94	426 (1)	52	6.9	85	132	15.1
5	4.8	3.1	3.3	97	51	161 (1)	—	1.8	91	−9	19.6
6	5.0	3.6	3.7	42	94	103 (2)	111	5.5	400	476	9.8
7	4.7	4.6	4.1	121	—	54 (1)	—	2.9	57	55	56.0
8	4.7	4.1	3.4	54	81	212 (3)	57	3.0	274	56	14.0
9	4.8	3.1	3.6	83	81	82 (2)	—	3.8	207	−65	13.6
10	2.9	4.0	2.6	68	94	118 (1)	—	—	4	4.7	—
11	4.5	4.2	4.2	85	75	—	102	3.4	89	137	6.3
12	5.0	3.3	3.7	68	44	—	33	4.3	264	61	9.1
13	4.8	4.7	4.2	95	—	111 (1)	86	5.0	64	283	14.0
14	5.0	—	4.7	—	88	—	48	4.3	144	—	8.8
15	4.4	4.5	3.7	44	45	63 (2)	42	—	293	52	10.2
16	4.8	4.3	3.7	—	—	—	—	4.3	38	178	5.9
17	4.7	4.0	3.7	57	58	92 (2)	40	2.6	384	75	11.5
18	4.1	4.0	3.1	—	—	169 (4)	—	—	—	—	—
19	4.6	3.6	3.8	—	58	137 (2)	51	—	—	—	—
20	4.6	3.5	4.2	—	99	75 (2)	—	—	—	—	—
21	4.5	3.6	4.2	—	88	64 (2)	47	—	—	—	—

Normal ranges: Ca (4.5–5.5 mEq/L), P (3.5–4.5 mg/dL), Albumin (3.8–4.8 g/dL), PTH (40–100 μEq/mL), 25-OH D (16–110 ng/dL), cAMP (2.1–5.9 μmol/G Creatinine), Ca/Cr (<200 mg/G), Hyp/Cr (<24 mg/G).
Normal range for Alkaline phosphatase: (1) = μM/min/L (20–90), (2) = μM/L (24–104), (3) = mU/mL (30–115), (4) = IU/L (20–104).
* Ca/Cr is recorded as mg/G.

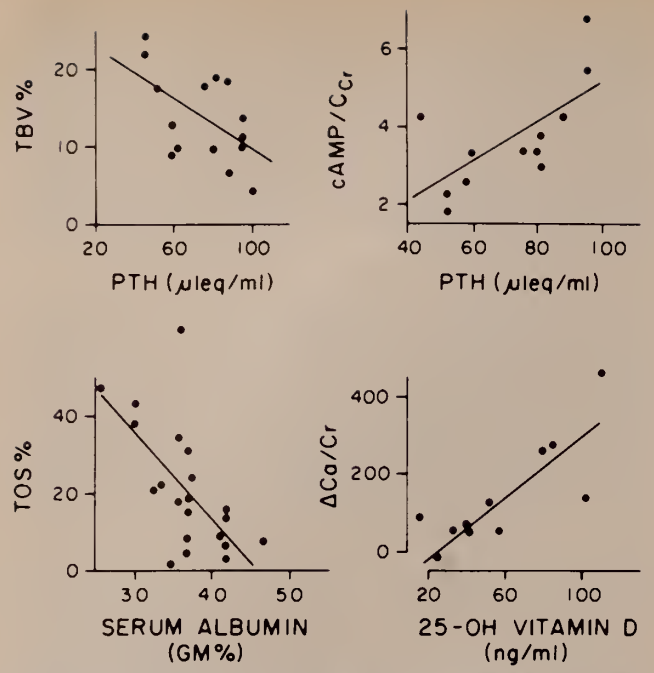

FIGURE 1. Correlations among bone biopsy parameters and biochemical measurement in patients with osteoporosis. Upper left: correlation of immunoreactive PTH with the percent trabecular bone volume (R = −.56, $P < .03$); upper right: correlation of immunoreactive PTH with urinary cyclic AMP (R = .62, $P < .04$); lower left: correlation of serum albumin with the percent trabecular osteoid surface (R = −.56, $P < .02$); lower right: correlation of serum 25-OH vitamin D levels with the increase in urinary calcium after an oral calcium load as expressed in milligrams per gram of creatinine (R = .80, $P < .01$).

both values probably do reflect the biologic activity of PTH.[17] Other biochemical values did not show any unexpected correlations.

Nonquantitative analysis of the bone biopsy specimens was carried out by at least two independent observers who were asked to provide a subjective pathologic diagnosis. They found mild to severe osteoporosis in all cases. In a number of instances the biopsy specimens were also considered to show a mild degree of osteomalacia, but no samples were encountered that showed markedly wide osteoid seams on qualitative analysis. On quantitative analysis, 17 of 21 patients had a 10 to 78% decrease in trabecular bone volume when compared with age- and sex-matched normal values as determined by Melson and Mosekilde (Table III).[18] The finding of normal values for the other four patients could be due to a sampling error. Of the 21 patients five had a substantial increase of TOS, but in no instance was the TOV of sufficient magnitude to make a clear cut diagnosis of osteomalacia. Moreover, available tetracycline labeling showed good mineralization fronts in all but one patient (No. 15) and in this patient there may have been an error in tetracycline administration. Thus the qualitative impression of mild to moderate osteomalacia (based on the appearance of increased surface osteoid) was not born out by any quantitative increase in relative osteoid volume or any gross impairment of mineralization fronts. Unfortunately, the one patient (No. 10) with hypocalcemia, marked fasting hypocalciuria, and elevated TOS did not have tetracycline labeling. Although a significant mineralization defect could not be ruled out, the TOV value in this patient was below that generally seen in osteomalacia.

A large number of correlations between the quantitative analysis of bone biopsy and biochemical measurements were carried out. Among the most interesting was an inverse correlation between immunoreactive PTH and TBV (R = −.56, $P < .03$)(Fig 1, upper left). In addition, there was an inverse correlation between the albumin concentration and the TOS (R = −.56, $P < .02$)(Fig 1, lower left). There were no correlations between age and any of the morphologic or biochemical parameters. This is not surprising since the study group was small and included a number of young individuals with metabolic bone disease.

Discussion

The study of metabolic bone disease is in its infancy. Diagnosis is usually made based on certain clinical and radiologic findings. Histomorphometric studies have shown that in certain bone disorders such as uremic bone disease there is not one discrete pathogenetic mechanism involved. It is far from clear whether the typical disorder of bone (eg, postmenopausal osteoporosis) involves one or many metabolic disorders.

In this group of patients no laboratory analyses or combinations thereof were found that could point to pathogenetic mechanisms in metabolic bone disease. Probably the most interesting correlation was that between PTH levels and TBV. All the PTH levels were within the normal range and yet high values did appear to be associated with low values for trabecular volume. Since a number of these patients had risk factors such as steroid use and gastrointestinal disease that might predispose to secondary hyperparathyroidism, this could be responsible for the correlation; however, examination of individual patients suggested that this was not the case. The role of PTH in the pathogenesis of osteoporosis has been discussed previously.[20-27] Parathyroid hormone levels have been found to be either high,[20-23] low,[24,25] or normal[26,27] in postmenopausal osteoporosis. Some investigators[22]—but not others[24]—have found a relationship between PTH levels and histologic evidence of increased bone resorption in patients with osteoporosis. Elevated PTH levels have also been shown to correlate with standard radiologic morphometric and photodensitometric evidence of osteoporosis.[21] Another correlation that might be expected from recent studies on vitamin D deficiency[28] is that 25-hydroxyvita-

TABLE III. Bone Biopsy Data

No.	TBV (%)	TOS (%)	TOV (%)
1	9.4*	63.8	7.4
2	9.6*	43.9	4.9
3	15.5	2.1	—
4	9.9*	35.1	4.8
5	17.4	21.2	2.3
6	11.3*	18.5	1.8
7	16.4*	9.5	1.0
8	18.9	22.1	1.0
9	12.3*	18.5	4.3
10	13.6*	49.4	5.7
11	17.8*	16.1	2.4
12	21.7*	13.8	1.7
13	10.6*	13.1	2.5
14	17.7*	6.0	1.3
15	24.1	8.6	0.5
16	13.5*	4.0	0.5
17	12.8*	31.0	7.8
18	10.9*	39.1	3.7
19	8.6*	22.7	2.7
20	3.9*	4.1	3.3
21	6.3*	5.2	1.5

TBV = Trabecular bone volume.
TOS = Trabecular osteoid surface.
TOV = Trabecular osteoid volume (see text).
* Decreased compared with normal values.[17]

min D appeared to be a reasonable indicator of impaired calcium absorption as measured by the response to an oral calcium load. It was of interest, however, that neither fasting urinary calcium nor the absolute increase in urinary calcium after an oral calcium load correlated with relative osteoid volume. The researchers were therefore unable to show any direct relationship between indices of intestinal calcium absorption and volume of unmineralized bone. Serum 25-hydroxyvitamin D levels have been shown to be elevated in postmenopausal osteoporosis[29] but have not been correlated with intestinal calcium absorption. Perhaps the most difficult aspect of the study to explain was the large amount of unmineralized osteoid surface in these samples that resulted in a frequent qualitative diagnosis of osteomalacia, although the normal osteoid volumes on quantitative analysis and presence of good tetracycline labeling indicated that there was no gross mineralization defect in these patients. Why were so many osteoid seams not fully mineralized? The best explanation for this finding is an increase in bone turnover, possibly accompanied by some delay in mineralization without any absolute defect in this process. However, many of these seams were covered with flattened cells and not with active osteoblasts. Moreover, there was no significant correlation with alkaline phosphatase. The fact that low albumin levels correlated with high values for the total amount of bone surface covered with osteoid seams may provide a clue. It is known that albumin is deposited into bone matrix during mineralization[30] and may, therefore, play a role in this process. These results do suggest further analysis of the possible role of nutritional deficiency in osteopenic states showing a high bone turnover.

Another possible mechanism for bone loss associated with increased turnover and increased PTH levels might be a renal leak of calcium, a mechanism implicated in postmenopausal osteoporosis.[29] A number of patients with fasting hypercalciuria were found in this group. Such patients might benefit from therapy with thiazide diuretics that decrease calcium excretion. The concept of increased bone turnover based on increased total osteoid seams requires extension and confirmation. Studies on the distribution of cells may aid in this regard. However, the researchers have found (as have others[9]) that the number of osteoclasts in these samples is small and variable so that it is difficult to assess resorption using this parameter. Assessment of resorption by the proportion of bone surface showing Howships lacunae is subjective, but may provide further information.

On the basis of these preliminary studies, it may be concluded that osteomalacia is relatively rare in individuals who do not show classic chemical findings for that disorder. Many of these patients had risk factors for metabolic bone disease such as gastrointestinal disorders,[31] prior gastric surgery,[32-34] liver disease,[35] alcohol abuse,[36] use of corticosteroids[37] or anticonvulsants,[38] poor nutrition,[39] diabetes mellitus,[40] rheumatoid arthritis,[41] and early menopause.[42] The mechanisms involved in the production of metabolic bone disease in these various disorders are complex. Although some of the risk factors are thought to predispose to osteomalacia, osteoporosis may be seen in many of these conditions.[34,35] That osteoporosis is the more common finding in patients with intestinal bypass,[34] for example, is intriguing. Although 25-hydroxyvitamin D levels are low,[34,43] classic osteomalacia is often not seen, perhaps because the malabsorption of protein results in decreased osteoblast function and decreased trabecular bone volume. Further prospective studies are necessary to test the significance of these findings in terms of pathogenesis of metabolic bone disease.

The researchers have been unable to find any shortcuts in the analysis of this heterogenous group of osteopenic patients. Although their technique of analyzing bone biopsy specimens provides useful information, bone biopsy with double tetracycline labeling is needed to define more clearly mineralization status.[44] Quantitative histomorphometric analysis is necessary to avoid erroneous subjective impressions. Calcium loading tests have shown so much variability that it seems unlikely they will provide adequate differentiation of patients with impaired calcium absorption. Therefore this test is no longer used in diagnosis; the researchers instead rely on quantitative histomorphometry using double tetracycline labeling in carefully selected patients with atypical bone disease.

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ACUTE OSTEOMYELITIS

The rapid increase of knowledge pertaining to surgical pathology has created a necessity for many changes in surgical nomenclature to render it consistent with our broader conceptions of the morbid processes. Thus, the earlier writers described several suppurative bone diseases and employed such terms as acute ostitis, endostitis, medulitis, periostitis and parostitis, all terms more or less misleading and incomplete in that they describe the progressive steps of a single disease, viz.: Acute suppuration of bone. It would appear, then, advisable to discard these names entirely, and apply the more comprehensive term,—acute osteomyelitis.

This disease furnishes the greater number of necrosis cases brought to the surgical clinics, and, in most instances, the fact that extensive necrosis has occurred is a reproach to modern medicine. It should not be looked upon as a specific disease, being nothing more than an abscess in a compact tissue. This disease is far from rare, and has a mortality greater than appendicitis, or typhoid fever, yet is but poorly understood by the general practitioner and is frequently overlooked until irreparable damage or even death have occurred.

ARTHUR W. BOOTH, MD
(*Trans Med Soc State NY* 1903;321)

Bordetella pertussis in New York State 1972–1982

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ABSTRACT. The number of specimens tested and those positive for *Bordetella pertussis* by the direct fluorescent antibody (DFA) test among patients in New York State increased progressively from 1972 to 1982. Of 6,749 specimens tested in the laboratory by the DFA test, 965 (14.3%) were positive overall, with 20 of 93 (21.5%) positive in 1972 and 141 of 1,212 (11.6%) positive in 1982. The percentage of positive test results fluctuated from a low of 7.9% in 1979 to a high of 25.7% in 1973. Most of the specimens received on transport media were also cultured for *B. pertussis*; of 917 cultured, 33 (3.6%) were positive. Of the total DFA-positive specimens 509 (52.7%) were from infants under 1 year of age. These summaries include data from seven outbreaks of pertussis during 1977, 1980, and 1982. Clinical data available for cases in 1982 demonstrate a close relationship between DFA positivity and clinically diagnosed pertussis, as well as support for the efficacy of vaccination.

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The cause of whooping cough, *Bordetella pertussis,* is a fastidious bacterium, and growth from clinical specimens requires immediate culture on special media. Recovery from the respiratory tract is highest during the first week of infection.[1,2] These circumstances make it difficult to recover the organism from patients by culture, particularly when the specimens are not taken during the acute stage of illness, when they are not delivered to the laboratory within a short time, or when they are taken from patients who have already received antibiotics. As a result pertussis cases are frequently based on clinical diagnosis.

The use of the direct fluorescent antibody (DFA) technique for the identification of *B. pertussis* in nasopharyngeal swabs has been a subject of controversy. This testing method has been found to be rapid, practical, specific, and sensitive.[1,3–9] However, other researchers prefer culture as a more specific indication of pertussis infection and to be more sensitive especially when plated on optimal media without delay.[10,11]

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Recently requests for testing—reflecting increased awareness or incidence of *B. pertussis*—has increased. Many laboratories do not routinely test for *B. pertussis* but rather forward specimens to a reference laboratory. Although improved transport media have been developed, obtaining a culture from these specimens is difficult.[12–14] Therefore there was a need to evaluate the DFA test as an indicator of clinical pertussis since it is frequently used in the diagnosis of pertussis infection in reference laboratories such as the one reported here.

From 1972 to 1982 the laboratory received 6,749 patient specimens for the identification of *B. pertussis.* These specimens were studied by DFA, and recovery of the bacteria from many specimens received on transport medium was attempted by culture. A clinical investigation was performed for reported cases in 1982 that allowed the comparison of DFA, culture, and clinical diagnosis for the detection of pertussis cases. In this report the findings, notably a progressive increase in requested tests for *B. pertussis,* an increase in the number detected by DFA during those 11 years, and the usefulness of DFA as an indication of clinical pertussis cases in specimens forwarded to a reference laboratory are summarized.

PATIENTS AND METHODS

The New York State Laboratory's transport outfit from 1972 to 1974 contained a 5-mL slant of Mishulow's medium[12] in a screw-capped tube, a Calgiswab (Inolex Division, American Can Company, Glenwood, IL) in its sealed envelope, and a history form. From 1975 to 1978 Mishulow's medium as modified by Jones and Kendrick (J-K)[13] was used as the transport medium. From 1979 to 1982 a modified Regan-Lowe (R-L) charcoal slant with 40 μg of cephalexin/mL, 10% horse blood, and 1.2% agar[14] was used as the transport medium.

Most swabs were taken from the nasopharynx; others were from the throat, nose, trachea, or bronchi. Most specimens were sent as smears while the rest were sent as swabs on the transport medium. Each swab was streaked on the transport slant and remained in contact with the base of the slant during transport by mail or messenger. Upon receipt in the laboratory the transport medium was incubated overnight at 37°C. The following day the swab was removed from the tube, streaked on isolation media, and then rinsed thoroughly in 1 mL of phosphate-buffered saline (PBS), pH 7.6. The PBS 7.6 was centrifuged, and smears were

TABLE I. Identification of *B. pertussis* by Direct Fluorescent Antibody (DFA) and Culture in New York State Exclusive of New York City From 1972 to 1982

	DFA			Culture	
Year	No. of specimens	No. positive	% positive	No. of specimens	No. positive
1972	93	20	21.5	2	2
1973	171	44	25.7	9	1
1974	308	73	23.7	56	1
1975	288	51	17.7	30	0
1976	241	22	9.1	17	1
1977	552	83	15.0	27	0
1978	897	132	14.7	37	1
1979	858	68	7.9	8	3
1980	1,259	220	17.5	129	8
1981	870	111	12.8	159	4
1982	1,212	141	11.6	443	12
Total	6,749	965	14.3	917	33 (3.6%)

made from the pellet. All smears, whether received as such or prepared in the laboratory, were fixed with 95% ethanol. Four smears were examined for each specimen.

The smears were tested by a standard DFA technique[15] with rabbit anti-*B. pertussis* serum conjugated with fluorescein isothiocyanate (Difco Laboratories, Detroit, MI). Three control films made from previously prepared, Merthiolate-killed suspensions of *B. pertussis, B. parapertussis,* and *B. bronchiseptica* were stained in the same manner. The smears were read on a Leitz fluorescence microscope equipped with a 200 W Osram mercury pressure bulb. Specimens received on transport medium that were negative by DFA on day 1 were reincubated at 37°C and retested on day 7. The same laboratory group, experienced in DFA microscopy, read the smears throughout the 11-year study.

During 1972 specimens were not cultured routinely. Thereafter all specimens positive by DFA were streaked as follows: 1973 to 1978, on Bordet-Gengou plates with and without penicillin (1 U/mL); 1979 to 1980, on R-L plates with and without cephalexin (40 μg/mL). During 1981 and 1982 all transport specimens, whether DFA-positive or negative, were streaked for isolation on R-L plates with and without cephalexin. The medium was inoculated with the original swab, and the plates were incubated at 37°C in 4% CO_2 for seven days. If typical colonies were found with a magnifying lens, they were fished for confirmation by biochemical tests.

Investigation of the cases in 1982 was performed by personnel of the Immunization Program of the Bureau of Communicable Disease Control of the New York State Department of Health. Cases were investigated for clinical symptoms, hospitalization, outcome, immune status, exposure history, and the status of other members of the household. Criteria for diagnosis were paroxysmal cough with whoop, positive culture, or positive DFA with persistent cough.

Results

The number of specimens tested and those positive for *B. pertussis* by DFA in clinical specimens received in the laboratory from all of New York State except New York City increased progressively from 20 of 93 in 1972 to 141 of 1,212 in 1982. The positive percentage varied from a low of 7.9% in 1979 to a high of 25.7% in 1973 (Table I). Although improved transport media were used as they became available, only 33 (3.6%) of 917 specimens cultured during this period yielded growth of *B. pertussis*. Of these 917 specimens 317 (34.6%) were DFA-positive for pertussis.

During 1981 and 1982, 602 transport specimens were tested by both DFA and culture. Sixteen specimens (2.7%) were both DFA and culture positive, 63 (10.5%) were DFA positive only, and none were culture positive only.

Smears prepared before submission to the laboratory and smears prepared from swabs on transport media showed similar rates of positivity. Of the 6,749 specimens received, 4,190 were sent as smears; 513 specimens (12.2%) were DFA-positive. Of the 2,001 specimens that were sent on transport media, 273 (13.6%) were DFA-positive. The remaining 558 specimens were received on other media such as Stuart, Bordet-Gengou, or Loeffler medium; 179 (32.1%) were DFA-positive. This latter group probably represents "highly probable cases" for which the physician submitted a specimen on available media. There were 249 instances during 1981 and 1982 where a prepared slide was received along with transport media on the same individual and of those 49 (19.7%) were DFA-positive. Eight specimens (3.2%) were DFA-positive from the transport only, 22 (8.9%) were DFA-positive from the slide only, and 19 (7.6%) were positive from both.

Nasopharyngeal specimens are those most commonly collected for the diagnosis of pertussis. Most of the specimens received in this study—4,664—were from the nasopharynx and 620 (13.3%) were DFA-positive. However, specimens from the nose (86 of 619, 13.9%), other sources such as throat and trachea (111 of 372, 29.8%), and those for which a source was not given (148 of 1,094, 13.5%) also yielded positive results.

Specimens from infants 1 to 6 months of age were most frequently DFA-positive (Table II). However, a striking number of laboratory-diagnosed cases occurred in persons greater than 10 years of age.

Neither sex had a significantly higher positivity rate: 15% (487/3323) for females and 14% (451/3225) for males. No sex was given for 201 specimens. There was a slight increase in the occurrence of DFA-positives from July to September (35.1%) and in cases reported to the Bureau of Communicable Disease Control from August to October (29.5%).

To determine whether the number of DFA-positive specimens reflected accurately the incidence of clinically diagnosed cases, the number of specimens DFA-positive for *B. pertussis* each year was compared with the number of clinical cases as determined after investigation by the Bureau of Communicable Disease Control of the New York State Department of Health (Fig 1). The numbers are closely correlated with a coefficient of .95 ($P < .01$) for the first ten years. In 1982 a majority of clinical cases from an outbreak in Cattaraugus County were not submitted for DFA testing, thus making any comparison invalid. The number of total specimens received was also significantly correlated with the number of DFA positives with a coefficient of .90 ($P < .01$) and with the number of clinical cases with a coefficient of .86 ($P < .01$) during the same time period.

Of 116 cases of *B. pertussis* infection detected by DFA in 1982 (excluding the Cattaraugus County outbreak) 100 were investigated by the Bureau of Communicable Disease control. Although it would be useful to compare these DFA-positive cases with DFA-negative cases, a complete investigation was not done on the majority of the DFA-negative individuals. Most of the DFA-positive patients had symptoms typical of pertussis infection: 93 cases had cough lasting from less than ten days to more than 40 days (30 of them between 10 and 20 days), 54% had a paroxysmal cough, 33% with whoop, and 31% had fever. Only seven patients were asymptomatic. Five of the asymptomatic cases received erythromycin after specimen collection and one patient received no antibiotics. The antibiotic treatment of the remaining case is unknown.

Most DFA-positive patients had not received a complete series of five diphtheria, pertussis, and tetanus (DPT) injections: 27 individuals had received none; 24, one; 12, two; 9, three; 13, four; 8, five;

TABLE II. Age Distribution of Patients Positive for *B. pertussis* by DFA, 1972 to 1982

Age	Number	Percent
Up to 30 d	37	3.8
1 to 6 mo	363	37.6
>6 to 12 mo	109	11.3
1 to 3 yr	138	14.3
>3 to 10 yr	108	11.2
Older	154	16.0
Not given	56	5.8
Total	965	100

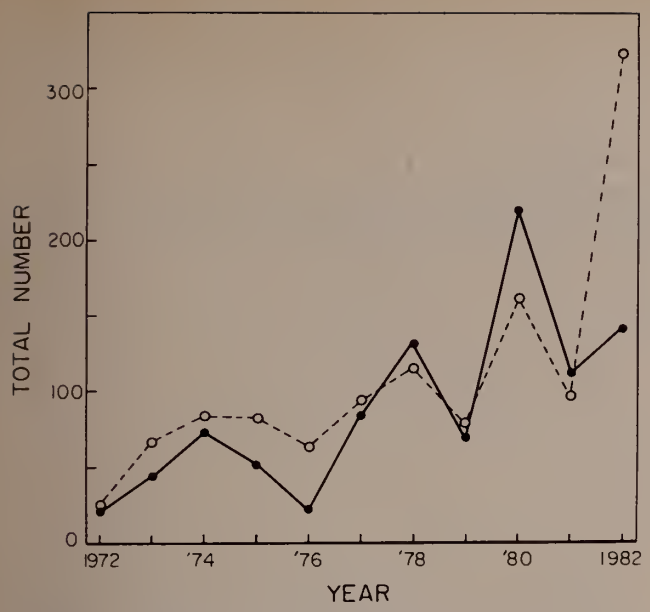

FIGURE 1. Correlation of DFA identification of *B. pertussis* in clinical specimens (•) with clinical cases identified by the Bureau of Communicable Disease Control (o). In 1982 the Cattaraugus County outbreak was responsible for 216 clinical cases, most of which were not tested by DFA.

and 7, unknown.

A high morbidity rate was associated with the DFA-positive cases. Of the 100 patients studied 43 were hospitalized for stays ranging up to more than 15 days. Thirty-eight nonhospitalized patients recovered without complications but 17 developed either pneumonia (8), otitis media (8), or convulsions (1).

Of specimens received from these 100 DFA-positive cases, 20 were submitted on R-L transport medium. These were tested by both DFA and culture, and eight (40%) were found to be culture-positive for *B. pertussis*. Two additional culture-positive specimens were recovered from submitted Bordet-Gengou media. Of these ten (ten of 22, 45%) culture-positive individuals, nine were symptomatic and one was asymptomatic. The number of culture positive cases is too small to allow for meaningful analysis of data on comparisons of timing of testing, or clinical and epidemiologic presentations between culture-positive, culture-negative, and DFA-positive patients.

During the study period there were seven outbreaks of pertussis (Table III). The most interesting outbreak occurred in 1982 in Cattaraugus County and affected primarily members of a religious community. Of 216 persons identified in the outbreak, 213 were symptomatic. Nasopharyngeal specimens from the three asymptomatic persons were DFA-positive, and one was culture-positive for *B. pertussis*. Most of the cases (46%) occurred in the 3 to 10 year age group. Many families in this outbreak had multiple cases of pertussis (32 families with four or more cases). The household secondary case attack rate overall was .43 and for children ≤10 years was .73.

None of the 216 individuals had received DPT immunization. Many also declined laboratory testing and treatment, even when several family members exhibited typical symptoms. Of the 77 (34 from investigated cases and 43 from noninvestigated cases) nasopharyngeal or nasal swabs taken for laboratory testing, 25 were DFA-positive, and of the 14 sent on transport media, two were culture-positive. Symptoms frequently seen were cough, 92%; paroxysmal cough, 88%; whoop, 84%; vomiting, 84%; and fever, 52%.

Discussion

An increase in the total number of specimens tested, the number of specimens positive by DFA for *B. pertussis*, and the number of pertussis cases reported to the Bureau of Communicable Disease Control was observed throughout the 11 years of this study; the former was conducted with the same laboratory procedures and experienced personnel. The significant correlation between the number of DFA-positive cases and the number of clinical cases with the total number of specimens could indicate that increased suspicion or awareness of pertussis has increased as well and is responsible for the increase in the number of pertussis cases. Most specimens are received from private physicians who submit specimens from clinically suspicious cases based on their own criteria and their awareness of the presence of pertussis in their area. An increased awareness could have resulted from the outbreaks or from an increase in endemic disease. Greater use of the New York State Laboratory may also contribute to the increase. However, the increase is probably real since morbidity associated with pertussis is generally so high that patients contact a physician and seek a diagnosis. Milder cases may be missed; therefore the cases reported here probably represent the minimum incidence of pertussis.

Comparison during 1982 for which the investigation of sporadic clinical cases was performed showed that DFA positivity reflected clinically diagnosed pertussis in almost all cases. *B. pertussis* infection was confirmed in 45% of the specimens received on improved transport media and culture media in spite of the fact that specimens are often delayed in transit for several days. The culture-positive individuals showed almost equal percentages with symptoms (nine of ten, 90%) as compared with DFA-positive individuals (93 of 100, 93%). Similarly, typical clinical pertussis symptoms were seen in more than 90% of the DFA-positive specimens from the Cattaraugus County outbreak. These observations lead the researchers to believe that DFA-positivity is a good indicator of *B. pertussis* infection, although a controlled study would be necessary for conclusive data.

An increased incidence in *B. pertussis* has been reported by other investigators.[16-20] The rise may reflect either reduced immunization of infants or failure to use the recommended dosage of DPT. The efficacy of the pertussis vaccine has been a subject of controversy in recent years, but later evidence indicates the clear benefit of routine childhood vaccination.[8,16,18,21-22] Investigation of an outbreak that occurred in the spring of 1980 in St. Lawrence County revealed a direct correlation between apparent vaccine efficacy as judged by the secondary case attack rate in households with a DFA-positive patient and the number of doses of DPT vaccine received. The secondary

TABLE III. Pertussis Outbreaks in New York State, 1972 to 1982*

Year	County	No. of specimens† Tested	DFA-positive
1977	Columbia	83	13
	Rensselaer	28	16
1980	St. Lawrence	378	93
	Otsego	83	13
1982	Westchester	41	10
	Orange	76	15
	Cattaraugus	77‡	25

* No outbreaks were reported for years 1972 to 1976, 1978 to 1979, and 1981.
† From patients and contacts.
‡ Many of the 213 symptomatic individuals declined to permit testing.

case attack rate for persons who received from none to two DPT injections was .75; for three DPT injections, .40; for four DPT injections, .21; and for five DPT injections, .08. Efficacy rose from 47% in persons receiving three doses to 57% in persons receiving four doses, and to 78% in persons receiving five doses (Douglas Campbell, unpublished data). This epidemiologic investigation and that of the Cattaraugus outbreak and sporadic cases in 1982 demonstrates the efficacy of vaccination, as well as the importance of the number of doses of DPT received.

Seven DFA-positive cases and one culture-positive case investigated in 1982 were asymptomatic. Other investigators have reported similar findings.[9,21,23] This may indicate individuals who were either treated early and did not develop symptoms or those who were colonized with *B. pertussis* without developing the disease. The DFA-positive culture negative individuals are frequently interpreted as false positives; however, they may represent individuals with prior antibiotic therapy or the specimens may have been delayed during transit to the laboratory and are culture negative as a result.

In the present series most of the cases of pertussis occurred in the summer, and 53% of all cases occurred in infants less than 1 year of age (60% in nonoutbreak cases). A similar age distribution was found in the Center for Disease Control's surveillance from 1979 to 1981[7] and from 1982 to 1983.[17] Although a preponderance of cases in females has been reported,[16] no significant difference was found in pertussis cases between the sexes.

Most specimens for *B. pertussis* culture received in a reference laboratory are delayed in transit from several hours to a few days, making the use of transport medium necessary. Although modified R-L transport medium is satisfactory, the organism often does not survive when the medium is unduly delayed in transport. Therefore most laboratories that perform both DFA and culture rely mainly on DFA for the identification of pertussis.[7,16] The results of DFA tests on specimens on transport medium or on slides may be reported within one day of receipt, whereas culturing takes several days for growth and biochemical identification. In this study recovery of the organism by culture was low, even though improved transport media were used as they became available.

Approximately two thirds of the specimens in this study were smears that had been made before submission to the laboratory. These smears showed a positivity rate equivalent to that of smears prepared from swabs on transport media. However, for smears and transport media received during 1981 and 1982 on the same individual the smears detected more DFA-positive (16.5%) than transport media (10.8%). However, the highest number of positive results were detected when both methods were employed (19.7%). Overgrowth by molds and other bacteria occurs and may be a factor. Smears are especially useful when transport medium is not available; however, it is always preferable to submit transport medium also, as it is suitable for both DFA and culture testing.

The frequency of laboratory identification of *B. pertussis* by DFA closely paralleled the number of clinical cases of pertussis found during investigation by the Bureau of Communicable Disease Control (Fig 1). Clinical information on DFA-positive cases for both a large outbreak and for sporadic cases in 1982 also supports the conclusion that DFA-positivity is closely correlated with clinical diagnosis of pertussis. In light of the lack of sensitivity in culturing for *B. pertussis,* DFA appears to be a reliable diagnostic test.

Addendum. The number of samples that were DFA-positive for *B. pertussis* was 75 of 1,089 (6.9%) specimens tested in 1983; 92 of 1,058 (8.7%) in 1984; and 85 of 931 (9.1%) specimens examined in the first ten months of 1985. Numbers of culture-positive were six, nine, and one respectively for 294 specimens cultured in 1983; 268 in 1984; and 191 in the first ten months in 1985. There was no major outbreak during the years 1983 to 1985.

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Magnesium deficiency and cardiac arrhythmias

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Numerous studies have documented an increased incidence of supraventricular and ventricular arrhythmias in patients with magnesium (Mg) deficiency.[1-3] Dyckner,[4] for example, found a higher incidence of ventricular tachycardia, ventricular fibrillation, atrial fibrillation, and supraventricular tachycardia in patients that were hypomagnesemic and who had acute myocardial infarction than in a reference group with normal serum Mg levels. Torsades de pointes has also been associated with the hypomagnesemic state.[1,5] In addition, both animal and clinical studies have shown that digitalis-induced arrhythmias are much more likely to occur in the presence of Mg deficiency.[6-8]

Magnesium deficiency is often overlooked as a cause of cardiac arrhythmias. These arrhythmias may be seen in a number of different clinical settings including valvular and coronary heart disease, alcoholism, and delirium tremens. This article will discuss diuretic use, acute myocardial infarction, and digitalis toxicity—three particularly well-studied situations in which magnesium deficiency may precipitate arrhythmias. Suggested mechanisms by which magnesium deficiency may influence cardiac irritability will also be reviewed, as well as possible therapeutic regimens.

MAGNESIUM DEFICIENCY

The term magnesium deficiency has been used by various researchers to denote a lowering in serum Mg, erythrocyte Mg content, myocardial cell Mg content, muscle cell Mg content, and whole body Mg. Strictly defined, magnesium deficiency refers to a depletion of whole body magnesium stores. However, the various indices that have been used correlate poorly with whole body magnesium stores. For example, magnesium deficiency may coexist with normal serum Mg levels, and hypomagnesemia may coexist with normal body stores of magnesium. In addition, serum Mg levels are known to be poor guides to myocardial Mg content. Instead they reflect bone Mg content and are frequently normal in the presence of severe muscle depletion.[9-11] Yet serum Mg levels are readily available, and they do provide some clinically relevant information.

When evaluating studies that have investigated magnesium and its relationship with cardiac arrhythmias, it is therefore important to note which index was used as an indication of magnesium deficiency. Since most clinical studies have used serum Mg levels as the index, this review will use the term magnesium deficiency to signify hypomagnesemia, unless specifically noted otherwise. Lastly, it should be noted that normal serum Mg levels are in the range of 1.4 to 2.2 mEq/L (0.7 to 1.1 mmol/L).

Diuretic use. Cardiac arrhythmias commonly arise during diuretic administration. These arrhythmias are often attributed to hypokalemia secondary to urinary loss of potassium (K). However, both loop diuretics (eg, furosemide) and distal tubule diuretics (eg, thiazides) have also been found to cause Mg loss during prolonged administration.[12-14] In one study, normal diuretic doses caused typical increases in urinary Mg loss of 25 to 50%.[15] The resulting hypomagnesemia was associated with decreased intracellular Mg and K concentrations as well as reciprocal increases in intracellular calcium (Ca) and sodium (Na) concentrations.[16]

Whang and associates[17] made two important points regarding hypomagnesemia that are particularly applicable in the setting of diuretic therapy: coexisting Mg and K deficiencies occur with greater frequency than is usually appreciated; and refractoriness of hypokalemia to K repletion should suggest the possibility of concurrent Mg and K depletion. Thus in patients with a history of prolonged diuretic administration, the routine measurement of serum Mg levels seems warranted. Without such measurement, magnesium deficiency may not be recognized, and cardiac arrhythmias that are refractory to conventional therapy may ensue.

Finally, a recent study by Dyckner and Wester[18] showed that the use of the K-sparing diuretics — amiloride, spironolactone, and triamterene — given in conjunction with conventional diuretics also provides a Mg-sparing effect. Consequently, the increased use of these drugs coupled with more frequent monitoring of serum Mg levels should lead to a decrease in the incidence of cardiac arrhythmias during prolonged diuretic use.

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Acute myocardial infarction. Studies have reported decreased serum Mg levels immediately following acute myocardial infarction.[4,19,20] These findings may be significant in light of the high incidence of life-threatening cardiac arrhythmias and sudden death during this time period. If a direct relationship between this transient hypomagnesemia and the occurrence of arrhythmias is confirmed, a case could be made for the prophylactic administration of magnesium after acute myocardial infarction.

Current studies are investigating the cause of this phenomenon. Initially, it was attributed to the use of diuretics in the period immediately following a myocardial infarction. However, Petersen and colleagues[21] excluded those patients taking diuretics and still found a significant reduction in serum Mg. Flink and coworkers[22] suggest that free fatty acids released at the time of infarction may bind serum Mg and result in the apparent decrease. Another suggestion, however, is that there is a transient intracellular influx of Mg at the time of myocardial infarction. This theory is being investigated by the examination of lymphocyte Mg content. Ryan and Ryan[23] reported that lymphocyte Mg content is a good index of cardiac muscle Mg levels. However, whatever the cause of this transient hypomagnesemia, its presence again emphasizes the importance of obtaining serum Mg levels in appropriate clinical situations. Without such studies magnesium deficiency may go unnoticed and untreated until clinically symptomatic.

Digitalis toxicity. Research has shown that digitalis toxicity is exacerbated by hypomagnesemia. Kim and associates[24] reported an increased incidence of arrhythmias associated with digitalis toxicity in hypomagnesemic patients. Significantly, animal studies have shown a lower threshold for digitalis toxicity in the presence of magnesium deficiency. In dogs, Seller and colleagues[8] found that hypomagnesemia lowered the cardiac threshold for atrial, junctional, and ventricular arrhythmias during the administration of digitalis glycoside. This sensitivity was corrected by the infusion of magnesium sulfate ($MgSO_4$). A possible mechanism for this change in threshold was suggested by Goldman and coworkers[25] who found that myocardial uptake of digoxin increased with magnesium deficiency. This suggests that magnesium deficiency, in the presence of normal digitalis levels, may potentiate cardiac arrhythmias. Digitalis use is thus another common clinical situation where frequent monitoring of serum Mg may avert potential arrhythmias.

Electrocardiographic changes. The arrhythmogenic potential of magnesium deficiency is reflected in the effects on the electrocardiogram. Observed changes include the following: prolongation of the P-R and Q-T intervals; ST-T abnormalities; flattening and widening of T waves; the occurrence of U waves; low voltage; and repolarization alternans.[1,26-27] Perhaps the most intriguing of these effects is the prolonged Q-T interval. This is thought to represent a disturbed and lengthened repolarization phase that may be caused by changes in the membrane transport of potassium. In addition to being one of the chief criteria for torsades de pointes, Q-T prolongation is also thought to predispose to aberrant conduction, reentry, and ventricular fibrillation.[4,27]

Another possible effect of magnesium deficiency is on oscillatory after-potentials. Oscillatory after-potentials are calcium-dependent and are known to play a role in causing the repetitive arrhythmias that are seen with digitalis toxicity. Dyckner and Wester[15] suggest a mechanism in which magnesium deficiency, through its effects on calcium, may facilitate the occurrence of oscillatory after-potentials and thus lead to some of the arrhythmias seen in digitalis toxicity.

Mechanisms of Magnesium Deficiency

Several different mechanisms have been proposed to explain the electrophysiologic changes seen in magnesium deficiency. These mechanisms include both direct and indirect effects on potassium and calcium metabolism. Cardiac arrhythmias probably arise from a combination of these effects. In addition, laboratory and clinical studies have shown that magnesium deficiency leads to decreased intracellular K and increased intracellular Ca. Thus, any proposed mechanism should attempt to explain these experimental findings.

Direct effects. The direct effects of magnesium deficiency are poorly delineated. Magnesium channels have not been identified in myocardial cell membranes, and Mg concentrations have little direct influence on myocardial membrane potentials. Rather, Na and K concentrations have been found to be the chief determinants of resting membrane potential. However, direct effects of Mg on K and Ca fluxes could account for electrophysiologic disturbances. Shine[28] reports that the effects of magnesium deficiency on potassium loss during digitalis administration may arise from a direct effect on K channels in the sarcolemmal membrane.

Other investigators have suggested that Mg may directly affect Ca fluxes.[6] Magnesium is thought to be a mimic /antagonist of Ca, possibly due to its structural similarity as a divalent cation. Suggested effects include the following: 1) competitive binding to Ca sites producing the appropriate physiologic response; 2) competition for Ca binding sites but not exerting an effect; and 3) displacing Ca from intracellular binding sites with a rise in intracellular Ca concentrations.[29]

Effects on potassium. Magnesium is an essential cofactor for Na-K adenosine triphosphatase (ATPase).[30] This enzyme is responsible for removing Na from myocardial cells and pumping in K to maintain resting membrane potential. Magnesium deficiency may adversely affect this pump, so that myocardial cells lose their ability to maintain normal intracellular K concentrations. This disturbance in electrolyte balance would explain the observation of increased intracellular concentrations of Na and hydrogen (H). The elevated extracellular K may be lost in the urine thereby causing hypokalemia. In addition, changes in intracellular/extracellular K have been found to lead to changes in resting membrane potential, K conductance, and repolarization.[31] These electrophysiologic disturbances are thought to increase cardiac irritability.

Effects on calcium. Magnesium is known to act as a Ca antagonist.[29] In fact, Mg administration causes clinical changes similar to those seen in the administration of a Ca blocking agent: peripheral vasodilation, flushing, decrease in blood pressure, and decrease in strength of cardiac con-

traction.[32] Since an excess of Mg has been shown to inhibit the effects of Ca, it has been suggested that Mg deficiency may potentiate the effects of Ca.

Iseri and French[33] identify four different mechanisms by which magnesium deficiency may affect calcium metabolism: failure to block Ca entry into myocardial cells; failure to extrude Ca out of cells via Mg-dependent Ca-ATPase activity; failure to prevent influx of Ca into the mitochondria; and failure of sarcoplasmic reticulum to sequestrate Ca.

Perhaps the best documented of these mechanisms is the effect of Mg on the Ca-ATPase pump. In the same way that Mg is a cofactor for Na-K ATPase, it has also been shown to perform a similar function in Ca-ATPase. A myocardial tissue deficiency of Mg may lead to an impaired ability to pump Ca out of the cell. Any change in function of Ca-ATPase could affect intracellular/extracellular Ca concentrations. This could, in turn, cause electrophysiologic disturbances.

Experimental evidence has shown that the plateau phase of the action potential may be shortened by Mg infusion when extracellular Ca concentration is low. Thus magnesium deficiency, in the presence of a low extracellular Ca concentration, may lead to a prolongation of the plateau phase. This mechanism could explain the prolonged Q-T interval seen in magnesium deficiency.

Therapy

Magnesium was first recognized as an antiarrhythmic agent in 1935, when Zwillinger used it to convert paroxysmal tachycardia to normal sinus rhythm.[34] After Zwillinger's initial experience, Boyd and Sherf[35] treated spontaneous arrhythmias by using 10 to 20 mL of 10% $MgSO_4$ with about a 50% success rate. In another report, Chadda and coworkers[2] describe a patient with hypomagnesemia and ventricular tachycardia that was unresponsive to K, procainamide, lidocaine, diphenylhydantoin, and cardiac pacing, but who converted with Mg infusion. A more recent study of 13 patients by Dyckner and Wester[32] shows a significant reduction in ventricular ectopic beats after infusion of 30 mmol $MgSO_4$ over 12 hours. This same study shows no decrease in ventricular ectopic beats after K infusion in the same patients.

Dyckner and Wester[32] also describe some important guidelines for Mg administration: 1) avoid treating patients with severe A-V or bifascicular blocks; 2) avoid treating patients with severe renal failure; and 3) give intravenous infusions extremely slowly. These guidelines should be kept in mind during any of the various treatment regimens for Mg administration.

Iseri and associates[36] currently recommend that when ventricular fibrillation or ventricular tachycardia cannot be controlled with lidocaine or other conventional drugs, an infusion of magnesium sulfate should be used. A dose of 2 to 3 g over one minute should be followed by 10 g over five hours. These doses are equivalent to 10 to 15 mL of 20% $MgSO_4$ (16 to 24 mEq) given slowly over one minute followed by 500 mL of 2% $MgSO_4$ (80 mEq) over five hours. The administration of an additional 500 mL of 2% $MgSO_4$ over ten hours is recommended for those patients who are severely depleted of magnesium. Finally, several recent reports suggest $MgSO_4$ infusion as an effective treatment for torsades de pointes.[37,38] Tzivoni and colleagues[37] use a bolus of 1 to 2 g of $MgSO_4$ followed by a continuous 24 hour infusion of 1.0 mg/min.

Although a number of reports have documented the successful suppression of arrhythmias with Mg administration, it should be noted that the efficacy of Mg therapy in large groups of patients has not been well studied. Magnesium infusions should be administered cautiously. Some useful clinical parameters include diminishing deep tendon reflexes at 2.5 to 2.6 mmol/L in serum, respiratory paralysis at about 5 mmol/L, and cardiac arrest at about 8 to 9 mmol/L. If Mg overdose does occur, its cardiac effects may respond to Ca administration or pacemaker therapy.[32]

Magnesium administration as a treatment for cardiac arrhythmias is not frequently used since magnesium deficiency usually goes unrecognized. Although hypomagnesemia may occur in the settings of diuretic use, acute myocardial infarction, and digitalis toxicity, serum Mg levels are not routinely obtained. With better recognition of Mg deficient states, therapeutic Mg administration for the correction of cardiac arrhythmias will become more commonplace. However, Mg infusion for the treatment of refractory cardiac arrhythmias is still experimental, and a well-designed trial to test the clinical efficacy of Mg administration is indicated.

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WATER AND ELECTROLYTES

It has been said, "The parenteral administration of water and electrolyte may be as life saving as the intravenous injection of blood and plasma." We physicians are charged with the responsibility of prescribing the correct oral or parenteral solution. We usually discharge this responsibility well as regards cellular requirements—for the appearance of a severely anemic patient mobilizes anxiety in most of us to the extent that we automatically think in terms of whole blood transfusions. Appearance may not be so obvious in a patient with dehydration. Nevertheless, it is our duty to recognize the condition and to ascertain if the dehydration is accompanied by acidosis or alkalosis or changes in concentration of electrolytes and water of either or both the intracellular or extracellular fluid compartments. As clinicians, it is our responsibility to prescribe the solution which will restore equilibrium. Because it is difficult to remember clearly the mechanisms which keep the volume of body water and electrolyte concentration fairly constant in health . . . [one must] review the more important influences which maintain normal equilibrium.

NORMAN S. MOORE, MD
(*NY State J Med* 1949; 49:620)

Heroin and medical reasoning: The power of analogy

GREGORY J. HIGBY, PHD

To argue by analogy is to infer from the fact that one thing is in some respects similar to another that the two things will also correspond in other, as yet unexamined, respects. In logic, reasoning by analogy is a form of non-demonstrative ... argument which, unlike induction proper, draws conclusions about the nature of a *single* unknown thing from information about a known thing or things which it to some extent resembles. It is a form of reasoning that is peculiarly liable to yield false conclusions from true premises.

Anthony Quinton
(*Harper Dictionary of Modern Thought*, 1977)

In rigorous medical reasoning, analogy may provide "clues to the solution [of a problem], but not the solution itself."[1] Students of physiology commonly hear that "the heart is like a pump, circulating nutritious and oxygenated blood throughout the body." But the heart is not a pump, any more than the spinal cord is a switchboard or the stomach a fuel tank. Analogy may be a useful tool for further understanding and a vehicle toward insight. Picturing human arteries as analogous to plumbing, for example, suggests certain causes for atherosclerosis. A model based on this scheme might prove helpful in designing research projects. But, of course, no one would suggest injecting lye into the arteries of a patient to "clean out his pipes." Analogy has its limits. Yet, as Edmond Murphy reminds us, it pervades even the most modern laboratory studies. When biomedical researchers use animals they base their conclusions on analogous relationships between humans and other living creatures.

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In therapeutics, perhaps the weakest part of medical practice throughout most of its history, analogy has been especially alluring. In his landmark study of the treatment of syphilis before 1900, Temkin noted that mercury had long been used to treat other disorders of the skin before its application against the French Pox: "The new disease, too, manifested itself upon the skin, and what was more natural than to apply the same remedy? Treatment by analogy has no rational basis.... Yet I wonder how many treatments then and now have been tried because of some resemblance between two diseases."[2] Ackerknecht concurs, referring to the "tremendous influence" of analogy in therapeutics.[3] These scholars emphasized analogies such as that above, where a drug effective against a disease with signs and symptoms similar to another disease is administered in a case of the latter. In this article the method by which the reputation of a drug may be significantly influenced by reasoning by analogy will be explored. In this case the drug is perhaps the most notorious of all: heroin.

In *Dark Paradise*, David Courtwright accurately summarizes the brief history of heroin's medicinal use in the United States. He implies that the drug's reputation as being nonaddictive lingered on (and misguided physicians for a decade) because it was usually prescribed in oral form. Although this interpretation is sound, additional factors—primarily the persuasiveness of analogy—contributed to the drug's dramatic rise and fall.[4]

It was at about the same time that hypodermic use of morphine became more popular in the United States (following the Civil War), and that researchers in Germany began to define and describe narcotic addiction. Edward Levinstein, inspired and stimulated by the work of Heinrich Laehr (circa 1872), gave the medical world a modern concept of addiction.[5] At roughly the same time, medici-

nal chemists investigated the chemical structure of morphine through molecular manipulation. In 1874, C. R. A. Wright synthesized a new derivative of morphine and called it "tetra-acetyl morphine"—what would later be called heroin.[6,7] Wright's interests were primarily chemical and not pharmacologic. However, he did give some of the new compound to an associate, who tested it on dogs and found it less active than morphine. This negative report probably discouraged others from trying the new drug.[8]

The fully acetylated derivative of morphine did not attract the attention of physicians until 1898 when the German physician-pharmacologist Heinrich Dreser published the results of his detailed study of the drug. Working with rabbits, Dresser showed that the drug slowed and deepened animal respiration. Its profound effects on respiration encouraged him to begin clinical trials immediately. Dreser and his associate at Elberfeld, Floret, reported great successes in treating respiratory ailments with diacetyl-morphine, produced under the name "heroin" by Friedrich Bayer and Company. Their findings indicated that physicians should prescribe heroin as a safer, more powerful version of codeine.[9,10]

Dreser and Floret based their conclusions on a two step analogy. Codeine, like digitalis and a few other drugs, possessed a selective action on an organ or organ system. Physicians had long recognized codeine's partial selectivity against cough. It could quell a cough almost as well as morphine and with fewer and less dramatic systemic effects such as opiate euphoria or habituation. Heroin possessed a selective activity on respiration similar to that of codeine, but apparently to an even more specific degree. Based on this line of reasoning—codeine is like digitalis and heroin is like codeine—Dreser and those who immediately followed him introduced heroin as a better and safer codeine and shrouded its full-blown opiate character.

The underlying idea of selectivity sprang from the centuries-old concept of drug specificity. Generally rejected by physicians under the domineering authority of Galenism, the idea that a specific drug could cure a specific ailment gained broader currency with the discovery of the efficacy of cinchona bark against malarial fever in the 17th century. The bark had little apparent effect on anyone without malaria, but possessed remarkable activity when administered to an individual with malaria. William Withering, at the end of the 18th century, demonstrated the specific efficacy of digitalis in the treatment of dropsy. According to Ackerknecht, medical practitioners of the mid-19th century were not especially fond of specificity and therefore prescribed digitalis for several disease states. After 1880 or so they returned eventually to a specific indication; prescribing the drug for cardiac insufficiency. For physicians of the late 19th century, digitalis exemplified a drug with a selective action (on the heart muscle) with few apparent systemic effects.[11]

In late 1898, Morris Manges, a New York physician, introduced heroin to America. He had read the papers of Dreser and Floret and tried heroin in his own practice at Mount Sinai Hospital. After a successful trial period of three months, he wrote his own report that was mainly a condensation of the German work up to November of 1898. It contained some key misconceptions of heroin's pharmacology that persisted for almost a decade. For example, Manges touted heroin as 100 times safer than codeine, and its action on respiration as nothing short of miraculous:

> Dreser showed that the respiratory curve after the administration of heroin proved that not only was the frequency of respiration lessened, but also that there was a decided prolongation of inspiration. In addition, after moderate doses, the volume of the individual respiration was increased, sometimes even doubled.[12]

According to Manges, heroin enables a patient with respiratory discomfort to breathe both easier and slower. The cough would subside and the patient would be more relaxed. The underlying disease could also be improved. Said Manges, "The capacity of each inspiration for work and for overcoming obstructions is considerably increased. Under such conditions it is out of the question to fear stagnation of secretory products."[12] In other words, the patient could breathe more strongly and thereby clear the bronchial passages of excess phlegm and other matter.

Regarding the other pharmacologic actions of this new drug, Manges concluded:

> As a general analgetic and in the treatment of abdominal disorders it was useless. On the other hand, at no time were there unpleasant after-effects from the drug, such as follow the use of morphine—i.e., nausea, vomiting, constipation, anorexia, etc. . . . Patients were able to go about attending their ordinary duties. Apparently there was no habituation to the drug.[12]

Thus heroin was introduced to the attention of American physicians as a respiratory specific: much less toxic than codeine, and without morphine's systemic side effects or habituation.

The next significant report on heroin came in March 1899 from Heinrick Leo, who revealed no new information but solidified the reputation of heroin as a respiratory specific. He enunciated the analogy implicit in the reasoning of Dreser and Floret when he said that "one can place heroin's action on respiratory function in parallel with the action of digitalis on the function of the heart."[13]

The analogy was soon reported in America in May 1899, when heroin's specific activity was again emphasized:

> Leo finds that, as a general narcotic, morphine and codein far exceed heroin in action. . . . It is in certain forms of dyspnea that heroin seems destined to fulfill its chief function. It tends to decrease the duration and force of the inspiration, comparable to the action of digitalis upon the heart. Upon this action depends the almost magic effect of heroin upon the dyspnea and cough of emphysema, chronic bronchitis, bronchial asthma, etc.[14]

With these optimistic reports in hand, American physicians—especially those who treated breathing problems—eagerly prescribed the new drug.[15-17] American pharmacologist Isaac Ott added his authority to heroin's growing reputation with a report on a controlled study of the drug. "As is seen it [heroin] has a very marked action upon the respiration-center, causing a great reduction in the number of respirations. . . . Hence, we may state that this drug has a specific action upon the center of respiration."[18]

Apparently confident that heroin possessed fewer dangers than other opiates because of its specificity, some

physicians began prescribing it for nonrespiratory complaints. This trend followed a pattern common with specifics like cinchona (quinine) and digitalis. Physicians were enthusiastic about having a drug that was demonstrably effective, and they used it for a wide range of indications. As Ackerknecht put it, "the specific becomes panacea."[18] In 1900, Morris Manges wrote another report on heroin that described its broader use. Not only did Manges summarize European information on heroin, but he published the results of a circular letter sent out to his colleagues. Placing the data in tabular form, Manges utilized 22 disease categories and gave the number of successes and failures attributed to heroin. Only 12 of the 22 disease states studied were respiratory ailments, suggesting that heroin's use had expanded significantly. However, of the 416 cases reported 371 (89%) were related to breathing difficulties. Physicians had tried heroin for many disease states, but only consistently used it in those of a respiratory nature. Manges, by 1900 a recognized authority on the drug, noted the other uses for heroin, but stressed that it was "distinctly inferior to morphine" in the treatment of pain and other systemic conditions.[19]

Since physicians viewed heroin as a more potent and safer drug than codeine, their continued belief in the drug's safety is understandable. When concerned clinicians compared morphine and heroin on an equivalent dose basis, they discovered that heroin did have greater respiratory activity than morphine. Comparative studies have also shown that heroin is from 50 to 100% higher in antitussive activity.[20] When given an antitussive dose of morphine, a coughing patient commonly experienced the normal opiate effects of analgesia and sedation. On the other hand, if the patient was given a low, effective oral dose of heroin, perhaps 1/24th grain, it produced little or no evidence of systemic opiate effects. Manges reported habituation in only 6 to 8% of cases, with the implication that those habituates had a susceptible constitution.[19]

Today addiction is the most interesting systemic effect of heroin. Physicians in the first few years of the 20th century overlooked the inherent addictive liability of heroin because of how it was prescribed. Patients given heroin or a prescription for a heroin preparation to relieve their respiratory distress rarely entered an institution unless quite ill. If their problem was an acute infectious disease, it soon ended and the heroin was discontinued before serious habituation could develop. At the other extreme was death from the disease. Chronic respiratory ailments caused by working conditions or tuberculosis were common. In these cases patients went home with their heroin prescriptions and took the drug for an extended period of time. Since they took it in oral form, habituation and tolerance to the heroin occurred at a relatively slow rate. There lies the crucial point: since heroin users had chronic conditions, there was no reason to stop taking the drug and withdrawal symptoms did not arise.

Respiratory drugs, like theophylline today, are generally taken orally for a long term—perhaps even life-long. This behavior contrasts sharply with the use of opiates for pain, especially in postoperative or posttraumatic pain, where patients improve and analgesics are discontinued. It is then that patients on high dose, injected opiates exhibit violent and frightening withdrawal symptoms. In the early years of the 20th century American physicians did not use heroin in that manner and after observing oral consumption for only a few years did not notice the addiction occurring. Moreover, when habituated heroin users did stop taking the drug, such as in cases of short supply, they usually attributed any discomfort to their disease state and not to the drug itself. Cough and shortness of breath would precede cramping, sweating, and other opiate withdrawal symptoms. Patient reports of such experiences reinforced their physicians's belief in the analogous relationship between digitalis and heroin: the former maintained proper heart function while the latter supported respiration.

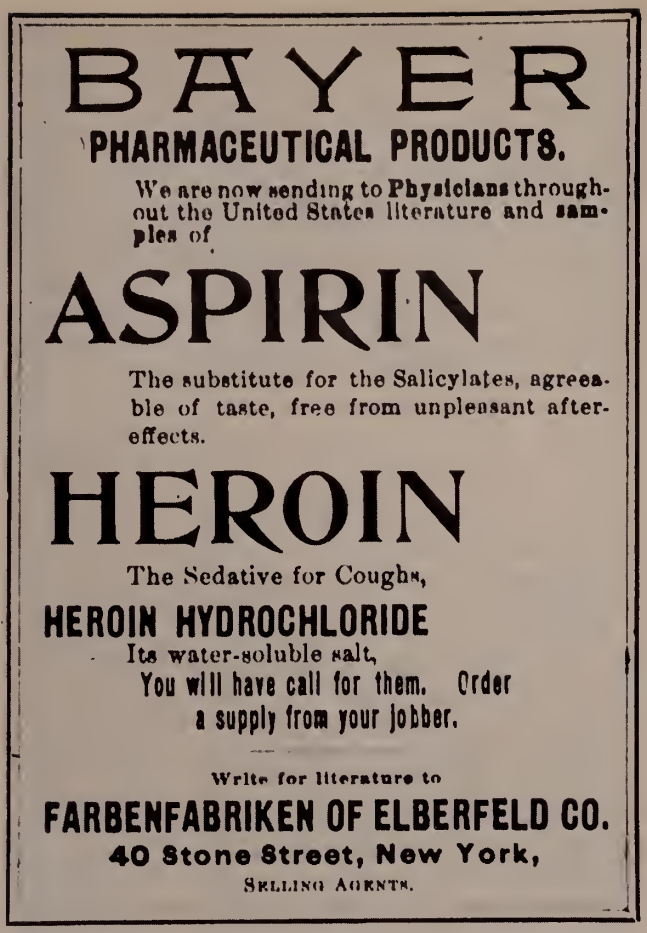
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FIGURE. The Bayer Company of Germany tried several marketing ploys to increase sales of its new drugs, aspirin and heroin. This advertisement appeared in pharmacy journals in 1900 encouraging pharmacists to stock up on these excellent products. (National Audiovisual Center, GSA, Washington, DC)

Manges, in his second article on heroin, also included a listing of the several new indications for the drug as suggested by European physicians. Stimulated by such listings, American physicians expanded their use of heroin during the next three years. Some doctors had mixed results and re-emphasized the old role of the drug for treatment of respiratory ailments.[21-24] However, other physicians found success when trying heroin in the treatment of severe pain. Samuel Brown and Erle Tompkins carried out a flawed but influential study of heroin in the treatment of postoperative pain. After treating 50 patients, Brown and Tompkins concluded, "Heroin is a safe, reliable analgesic,

one which can be repeated if necessary without producing habit or doing harm in any way."[25] Norman Geis of Brooklyn, New York, successfully relieved the pain of a terminally ill cancer patient with heroin. After his experience, Geis wrote that heroin was "destined to take the place of morphine in cases in which that drug is given for the relief of pain only."[26-28] By the peak of heroin's popularity in late 1902, some physicians had advocated it for a wide range of conditions including diabetes, insanity, epilepsy, dysmenorrhea, and hemorrhoids.[19,29,30]

After a few years of medical use, the addictive qualities of heroin began to surface. Physicians who treated drug addicts began to see heroin users at their doors.[31] Pharmacists witnessed the great disappointment expressed by persons who found heroin out of stock at their favorite stores.[32,33] To American physicians heroin was still a respiratory drug—an effective cough medicine—not a systemic opiate. If it were addicting, then it was not any worse than codeine.[34] Reports of addiction referred to the weakness of the victim or to prolonged administration of the drug.[35]

Physicians started to discontinue their use of heroin in the years before 1910 not so much for the addictive potential as for the supposed toxicity. Heroin the respiratory specific became heroin the respiratory poison. The explanation for this remarkable turnabout in reputation is tied both to the drug's former reputation as a specific and to the experiences of those physicians who treated heroin overdoses. As previously outlined, physicians often compared heroin's specific action on respiration to that of digitalis on the heart. Both drugs slowed and strengthened at their sites of action. Because of digitalis' pharmacology it was usually prescribed as a life-long maintenance drug that supported the heart. Heroin, by the power of analogy, supported the respiration of those with serious breathing problems. Heroin had become, in the hands of some practitioners, a maintenance drug.

Physicians who treated heroin addicts through abrupt withdrawal noticed that many of them experienced serious sequelae; some died in respiratory collapse.[36,37] This finding further strengthened heroin's reputation as a support of breathing. When this became common knowledge, however, physicians were faced with a difficult question: what should be done with those who relied on the drug?

An answer was forthcoming. During 1906 and 1907 the American Medical Associaton (AMA) prepared a new annual publication to inform their membership about new and nonofficial drugs on the market. Periodically in their *Journal*, proposed monographs on the new medicines would be presented for "criticisms and corrections . . . before final acceptance and publication in book form." The following is part of the proposed heroin monograph:

> The habit is readily formed and leads to the most deplorable results. . . . [Heroin] lessens irritability of the respiratory center, thus allaying cough, but does not depress the respiration as much as morphine. On withdrawing habitues there is said to be a tendency to respiratory failure which may be dangerous. . . . To avoid respiratory failure in the treatment of heroin addiction, it has been suggested to substitute morphine for the heroin and then treat the patient for morphine addiction.[36]

Apparently no readers raised any serious objections to this monograph and it appeared in the first edition of the AMA's *New and Non-Official Remedies* (1907). Thus among some American physicians heroin had changed from being a respiratory specific to being a respiratory poison. Heroin had replaced morphine as the most dangerous medicinal opiate, not because of its tantalizing euphoric effects but because it produced serious respiratory dependence.

The above evaluation of heroin in 1907 was not universally held. Physicians who relied on less current sources of information, such as textbooks, received a mixed assessment of heroin. Horatio C. Wood, Jr considered heroin a mild opiate with little or no addictive liability.[38] William Osler still equated its activity with that of codeine.[39]

In 1911 a group of surgeons in Kentucky met to discuss their concerns regarding the dangers of heroin in the treatment of postoperative pain. No consensus could be reached. One surgeon claimed that he had "never seen a contracted pupil or any other physiological action characteristic of the morphine group." [40] At the other extreme, the discussion leader concluded that because of the depressing effects on respiration, heroin was "one of the most toxic of the morphine group." [40] Another doctor warned of the addictiveness and asked his colleagues to see that "harmless preparations of opium are dreamed of by empirists and manufacturers, but do not exist." [40]

This discussion reveals the diversity of opinions held by physicians in regard to heroin and its dangers, ranging from totally safe to highly addictive. However, these latter dangers were still associated with the drug's supposed pharmacology that was rarely linked directly with the parent drug, morphine. In late 1911, the connections between heroin and respiratory specificity were finally broken when two physicians compared heroin with morphine objectively.[41] Yet even this more realistic analogy prevented the rational evaluation of diacetyl-morphine.

During the early years of the 20th century, narcotic addiction had become a social issue and the unfortunate morphine habitué had become the dangerous drug fiend. Society at large felt menaced by narcotic-maddened individuals. Drug addiction turned into a scapegoat for some of the society's ills.[42] When Brooks and Mixell reported that morphine addicts were turning to heroin because it provided more euphoria, the stage was set for the eventual prohibition of heroin.

Near the end of 1912, an article published in the *Journal of the American Medical Association* dealt a strong blow to heroin's sagging reputation. The author, John Phillips of Cleveland, alerted his fellow physicians to the increasing incidence of a new form of drug abuse: heroin sniffing.[43] This technique, supposedly copied from cocaine abusers, became a preferred method of administration among heroin addicts. Differing from previous reports of heroin addiction, Phillips documented cases of heroin abuse as the primary culprit and not the alternative drug of a morphine or cocaine user. He provided case histories of tragedies that resulted from physicians believing in the long-term safety of heroin. Several victims had been reformed morphine addicts who had requested opiate-free medicines from their doctors. Above all, Phillips regretted that misconceptions about the pharmacology of heroin had permitted the drug to escape legal restrictions. While state law often required a prescription for other narcotics,

heroin could be bought over the counter from any druggist. As the street price of morphine rose, 100 1/12 grain heroin tablets sold for less than a dollar.[43]

As other reports of heroin sniffing reached the press after 1912, the drug's reputation became connected with cocaine fiends, tenderloin districts, and dissipation. Since addicts of cocaine and morphine were switching to heroin, physicians were convinced that it must be a more dangerous and more devilish drug.[44,45]

Yet as several historians have pointed out, heroin's reputation suffered for a variety of reasons not connected to its pharmacologic properties. As mentioned, in the years before the Harrison Narcotic Act (1914) state and local laws usually failed to restrict the sale of heroin, making it more available to abusers than morphine, cocaine, or even codeine.[46] Secondly, the World War and subsequent anti-German sentiment dominated America in the years following the passage of the Harrison Act. Incredible stories swept across the country of German agents smuggling heroin into army camps or giving children heroin-laced candies on playgrounds. Through the popular press the public had learned that heroin enslaved rapidly and that it was, of course, of German origin.[47]

A third reason for the restriction of the sale of heroin was that its pharmaceutical properties made it superior to morphine as a street drug. It was three to four times as strong as morphine and therefore easier to hide; its more amorphous crystalline structure made heroin much easier to adulterate than morphine; and its higher water solubility made heroin easier to inject than morphine. Moreover, addicts could swallow, smoke, or sniff heroin, while injection was the only dependable option with morphine.

Influenced by both the medical and popular press, most physicians stopped prescribing heroin from about 1915 on.[4,48,49] In December 1916 the Surgeon General of the US Public Health Service stated that heroin served no purpose that could not "be accomplished by other agents . . . as effectively and without the attendant possibility of great disaster."[50] Ironically, diacetyl-morphine had just become official in September 1916 in the ninth revision of the *United States Pharmacopeia*. Since *USP* IX was six years late, it reflected the attitudes of American medicine and pharmacy of around 1910.[51] At that time American physicians tried to distance themselves as much as possible from iatrogenic drug addiction, especially to heroin.[52] When governmental officials called for the prohibition of diacetyl-morphine, little objection came from within the medical community.[52,53] By the early 1920s, heroin comprised only about 1 to 2% of the total opiate market in the United States.[54] When heroin was effectively banned in 1924, its medicinal history in the United States essentially ended.

This article has attempted to answer more fully a perplexing question first addressed by Terry and Pellens in their monumental study, *The Opium Problem*, and answered by several historians—most recently David Courtwright. Why did American physicians confidently prescribe heroin for more than a decade without noticing the addictive characteristics?[54] Building on Courtwright's observation that heroin was used almost entirely for respiratory ailments, the premises on which rested the medical reasoning of early 20th century American physicians regarding diacetyl-morphine have been shown. Blinded by the powerful analogies drawn between heroin and other supposed specifics, physicians used heroin as they would codeine and interpreted adverse effects of the drug accordingly. Betrayed in a sense by both eminent pharmacologists and drug manufacturers alike, physicians reacted strongly when their old specific became the drug of choice for drug addicts. In less than 20 years, heroin went from being a respiratory specific to a respiratory poison to a "devil drug." Caught up in reasoning based on comparisons to older drugs, American medicine and society at large transformed this faithful servant into a whipping boy. The drug itself has never changed.

See also pp 121–122.

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THE HISTORY OF MEDICAL TREATMENT IN EARLY AMERICA
A SYMPOSIUM
Friday, April 18, 1986

Anatomical drawing of a model with two skeletons by Burgess, London, circa 1755–1760. (From the collection of Pennsylvania Hospital, Philadelphia.)

Fraunces Tavern Museum, located on Pearl Street in lower Manhattan, will be conducting a one-day symposium entitled "Interpreting Medical History in Early America," which is provided in Part by funding by the New York State Council on the Arts and the New York Council for the Humanities. This symposium will be held in conjunction with a special exhibition entitled, "The Healing Arts in Early America," which is a major loan exhibition on disease and medical treatment in 17th and 18th century America. Registration information may be obtained by contacting Fraunces Tavern Museum, 54 Pearl St, New York, NY 10004. Tel: (212) 425-1778.

Hooper's Female Pills—wooden box with medicine, London, late 19th century. (From the collection of the National Museum of American History, Smithsonian Institution, Washington, DC.)

Evaluation of a child with a possible bleeding disorder

RICHARD H. SILLS, MD

Many normal children manifest symptoms suggestive of a bleeding disorder, such as epistaxis and bruising. In response to the parents' concerns, one must initially determine whether the child is normal or has an underlying bleeding disorder. If a careful clinical evaluation suggests that an underlying bleeding disorder is a reasonable possibility, a limited number of reliable screening tests should be performed. The presence of a bleeding disorder may then be confirmed and a definitive diagnosis established in an efficient and logical manner.

PHYSIOLOGY OF HEMOSTASIS

There are well established diagnostic approaches to bleeding disorders. Their use is contingent on a knowledge of the physiology of hemostasis[1-3] (Fig 1).

For bleeding to occur, blood vessels and their endothelial linings must be disrupted. Within seconds, circulating platelets adhere to collagen in the exposed subendothelium. This adhesion is mediated by a portion of the factor VIII molecular complex called von Willebrand's factor (VIII/vWF). This forms a bridge between platelets and collagen, allowing a monolayer of platelets to cover the subendothelium. This platelet monolayer is not hemostatic. However, the adhered platelets then release their stored pools of adenosine diphosphate (ADP) and other substances that induce the platelets to become sticky and to aggregate to each other. Circulating platelets then aggregate to the platelet monlayer and, in turn, release their own ADP. This chain reaction of platelet aggregation results in a hemostatic platelet plug within one to three minutes.

Fibrin formation is not necessary for initial hemostasis in small blood vessels, but it does prevent the later breakdown of the hemostatic plug.[3,4] In larger vessels, fibrin formation in and around the platelet plug is required to attain hemostasis initially.[5,6] The exposure of circulating blood to tissue thromboplastin (tissue juice) and to the subendothelium during vascular injury triggers the extrinsic and intrinsic pathways of fibrin formation respectively. Inactivated serine proteases (factors XII, XI, IX, VII, X, and II) are activated and in turn activate the successive inactive serine proteases along the pathway. The extrinsic pathway begins with the activation of factor VII while the intrinsic system begins with the activation of factors XII and XI. These reactions occur in and around the platelet plug partly because the aggregating platelets provide the platelet membrane phospholipid that is required for fibrin formation.

Activation of both the extrinsic and intrinsic pathways are necessary for adequate thrombin formation.[5] Thrombin then converts fibrinogen into an electrostatically bound fibrin polymer mesh that temporarily strengthens and stabilizes the hemostatic platelet plug. Factor XIII finally forms covalent bonds within the fibrin mesh to provide greater stability.

Causes of excessive bleeding. In evaluating the patient with a potential bleeding disorder, the first question to consider is what may cause the excessive bleeding. There are four possible types of defects: vascular defects; disorders in platelet plug formation; abnormalities in fibrin formation; and excessive trauma.

Vascular disorders are frequently overlooked as causing excessive bleeding. Increased vascular fragility may cause bleeding to occur so readily that a normal hemostatic system cannot compensate. The common causes of vascular

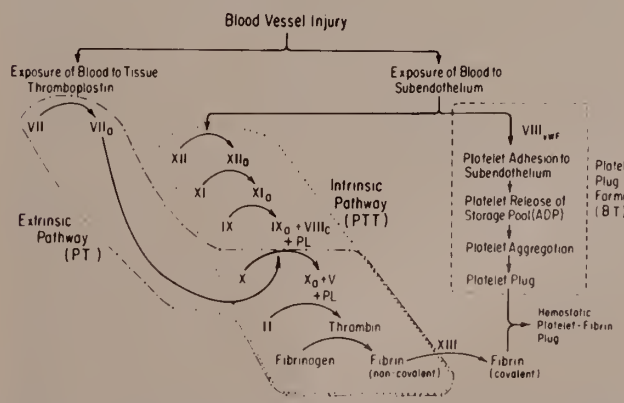

FIGURE 1. Schematic representation of the physiology of hemostasis. The circumscribed pathways are labelled with their respective screening tests in parentheses. PT = prothrombin time, PTT = partial thromboplastin time, BT = bleeding time, PL = platelet phospholipid, a = activated form of clotting factor, ADP = adenosine diphosphate, VIII_c = coagulant activity of factor VIII, VIIIvWF = von Willebrand's factor activity of factor VIII.

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defects of childhood include viral infections, Schönlein-Henoch purpura, and bacterial infections such as meningococcemia. Inherited vascular disorders such as hereditary telangiectasia are much less common. All of these diseases may usually be recognized on a clinical basis and do not often present a diagnostic problem.

Disorders in platelet plug formation may be due to a quantitative defect, as in thrombocytopenia, or to a qualitative defect of platelet function. Thrombocytopenia in children is usually acquired. Immune thrombocytopenic purpura (ITP) is most frequent. Other common causes include infections, bone marrow replacement by infiltration with cancer cells and, in critically ill patients, disseminated intravascular coagulation.

Platelet dysfunctions may be either acquired or inherited. Acquired platelet dysfunctions are usually directly related to intake of drugs, such as aspirin, other nonsteroidal antiinflammatory agents, or antibiotics. Platelet dysfunctions are much less frequently related to acquired disorders such as uremia. Inherited dysfunctions are common. These include von Willebrand's disease, which is the most common hereditary bleeding disorder.[5,7,8] Other inherited platelet dysfunctions, which include storage pool disease and aspirin-like defects, are now also recognized to be fairly common disorders.[7,9,10]

Abnormalities of fibrin formation occur in several diseases. Inherited disorders include von Willebrand's disease, which is usually associated with a deficiency of factor VIII:C as well as a platelet dysfunction. The hemophilias are less common but usually much more severe. Acquired disorders associated with abnormalities of fibrin formation encountered among children include liver disease, disseminated intravascular coagulation, vitamin K deficiency, and the use of anticoagulants.

Excessive bleeding may also be the result of trauma. Even a normal hemostatic mechanism will fail in the face of excessive trauma. Child abuse must always be considered in children who manifest excessive bruising.

Evaluation of Bleeding Disorders

The most frequent clinical question that arises is not the nature of the underlying bleeding disorder. Rather one is faced with determining whether or not there is a bleeding disorder at all. It can be difficult to answer this question, especially in children. Increased bruising in toddlers is most often the result of their expected frequent falls. Epistaxis in children results more often from nose picking, colds, and dry heating in winter than from coagulation disorders. The clinical evaluation plays a role in deciding whether or not a true hemostatic problem exists. Table I outlines historical information that should be obtained when determining whether a bleeding disorder is present. The absence of a significant history of bleeding in an infant does not rule out a congenital hemostatic disorder. von Willebrand's disease rarely presents in infancy and even the majority of very young children with hemophilia go unrecognized for months in the absence of a family history.

The physical examination is vital in confirming those physical findings reported in the history and in demonstrating findings of underlying systemic disorders. Examination for lymphadenopathy, hepatosplenomegaly, joint abnormalities, and signs of hepatic disease is imperative.

TABLE I. Historical Information For Evaluating a Child With a Possible Bleeding Disorder

General
Excessive bruising especially without trauma (often reported in patients without bleeding disorders)
Bruises over 5 to 6 cm in diameter, petechiae
Recurrent or severe epistaxis (frequent false positive responses)
Hematemesis, hematochezia, melena
Menorrhagia, postpartum bleeding, hematuria
Duration of bleeding history (congenital versus acquired)
Symptoms over many years or since infancy?
Past challenges to hemostasis
Bleeding with eruption of primary dentition
Gingival bleeding with tooth brushing (may be due to poor hygiene)
Excessive bleeding with significant trauma
Surgical procedures, especially tonsillectomy, dental extractions, and circumcision (the latter less often associated with bleeding)
Does aspirin exacerbate bleeding manifestations?
Medical history
Underlying disorders (collagen vascular, liver, and renal diseases; infections; malabsorption; hypotension; malignancies)
History of iron deficiency or transfusions suggesting blood loss
Medications
Note patients often do not consider aspirin a drug (ask specifically about aspirin ingestion within seven to ten days; check over-the-counter combination drugs that may contain aspirin)
Nonsteroidal anti-inflammatory drugs
Family history
Often difficult to assess
Carefully repeat all of above questions for the rest of the family —don't just ask if anyone else is a bleeder
If family history is positive, does it fit a genetic pattern (autosomal dominant or recessive, sex-linked recessive)?

If the history and physical examination suggest the presence of an underlying bleeding disorder, the next step is to differentiate which of the four categories of coagulopathies is present. Table II outlines clinical criteria that may be used to determine the type of hemostatic defect even before proceeding to laboratory studies.

Once the clinical evaluation is complete, the next decision is whether any laboratory evaluation is necessary. Children with a few small bruises over the tibias or with occasional, mild epistaxis do not require further evaluation if the child is judged clinically to be otherwise normal.

If the clinical evaluation raises any significant suspicion of a bleeding disorder, laboratory investigation is necessary. The key to a proper work-up is to choose a limited number of reliable screening tests that are both sensitive and specific.

Preliminary data should include a complete blood count and examination of the blood smear. These preliminary tests help to identify a wide variety of disorders including iron deficiency anemia due to blood loss, microangiopathic hemolytic anemia associated with thrombocytopenia, and pancytopenia due to bone marrow aplasia or replacement. Platelet number should be estimated and platelet morphology evaluated.

Further screening tests should examine the four general categories of hemostatic defects: vascular disorders, defects in platelet plug formation, defects in fibrin formation, and trauma.

Vascular disorders. There are no specific laboratory

TABLE II. Clinical Criteria For Differentiating the Type of Hemostatic Defect

Capillary
Cutaneous bleeding (mainly petechiae and purpura) common
Look for specific pattern (eg, Schönlein-Henoch purpura) or types (telangiectasia, angiomas) of vascular lesions
Lesions tend to be dependent in distribution
Petechiae tend to be raised
Platelet plug formation abnormality
Classic lesions are petechiae and purpura that are flat, appear in crops in areas of trauma, and tend not to be dependent
Since initial platelet plug formation is inadequate, bleeding tends to be immediate
Superficial cuts and abrasions bleed profusely but local pressure controls it (since pressure allows time for fibrin clot to form)
Skin and mucous membrane bleeding (gastrointestinal, hematuria, menorrhagia) is common while hemathroses and deep hematomas are rare
Fibrin formation abnormality
Ecchymoses and deep hematomas that are raised and spreading are common lesions
Initial hemostasis usually adequate (normal platelet plug) but bleeding recurs minutes or hours later when fibrin fails to maintain it
Local pressure does not permanently control because fibrin-deficient platelet plug is too unstable
Superficial cuts tend not to bleed because platelet plug is adequate
Deep muscle and joint bleeding is common
Late umbilical cord bleeding suggests factor XIII deficiency
Trauma
Bruises in exposed areas
Look for "non-physiologic" patterns of bruising seen in child abuse

studies that will accurately identify the presence or absence of a vascular disorder. The bleeding time is above all a measure of platelet plug formation and is usually normal in vascular disorders.[11] The capillary fragility (Rumpel-Leede) test is of doubtful value because of frequent false negative and false positive results; at least 8% of normal persons have a positive test. The diagnosis of a vascular disorder is therefore established on the basis of clinical criteria, such as the presence of Schönlein-Henoch purpura or a viral infection, and the absence of evidence indicating another type of bleeding disorder.

Defects in platelet plug formation. Such disorders consist of quantitative defects, as in thrombocytopenia, and qualitative defects, as in cases of platelet dysfunction.

The diagnosis of thrombocytopenia may be made on blood smear. However, estimates of platelet numbers made by examination of the blood smear, especially in relatively inexperienced hands, may be inaccurate. Thus, a direct platelet count should be obtained to confirm thrombocytopenia.

The only useful and accurate screening test of platelet function is the bleeding time. This involves creating a superficial vertical cut (less than 1 mm deep) into the subcutaneous tissues of the volar surface of the forearm. In children, this is easily done using a spring-loaded device (Simplate, General Diagnostics). The test is performed using a sphygmomanometer to create a positive venous pressure of 40 mm Hg. Since the wound involves only small, superficial subcutaneous blood vessels, the platelet plug is adequate for producing hemostasis. The bleeding time will be normal even in severe defects in fibrin formation unless platelet plug formation is also affected. However, moderate to severe thrombocytopenia will prolong the bleeding time by impairing platelet plug formation. Therefore a platelet count should be done before determining bleeding time since the presence of thrombocytopenia will negate the usefulness of the bleeding time.

The key to an accurate bleeding time is meticulous standardization. Considering the infrequency with which this test is done in a practitioner's office, the bleeding time is best performed in a hematology laboratory. Each laboratory must also establish its own normal range (usually up to five to eight minutes), as should be done with all coagulation studies. Small scars may form; the test should be avoided in patients who have a history of keloid formation. To minimize scarring, the edges of the wound should be taped in close apposition for 24 to 48 hours. Before a single prolonged bleeding time may be considered significant, the presence of a prolongation should be confirmed no less than seven to ten days later.

The ingestion of aspirin within seven to ten days prior to the test will prolong the bleeding time through the inhibition of platelet storage pool release. Aspirin ingestion may be used to increase the sensitivity of the bleeding time by providing a "stress test" of platelet function. The bleeding time will normally increase by four to six minutes two hours after the ingestion of aspirin, 15 mg/kg of body weight, with a maximum dose of 650 mg. Patients with mild platelet dysfunction may have normal or borderline bleeding times; however, their "post-aspirin" bleeding times are usually markedly prolonged beyond the normal increase. Although the usefulness of the post-aspirin bleeding time varies in different circumstances, it can identify mild platelet dysfunctions that are missed with a routine bleeding time.[7-9,12] This test should be used for patients with findings suggestive of a bleeding diathesis who otherwise have normal screening tests—including a routine bleeding time—and in patients suspected of having a bleeding tendency and a borderline or only minimally prolonged routine bleeding time. A normal post-aspirin bleeding time in these situations helps confirm or exclude the possibility of a platelet dysfunction. If the routine bleeding time is clearly prolonged, the post-aspirin bleeding time will provide no further information and the aspirin may exacerbate the underlying bleeding disorder. Specific platelet function studies performed under the supervision of a hematologist are then indicated.

Defects of fibrin formation. The prothrombin time (PT) and the partial thromboplastin time (PTT) are excellent screening studies for detecting abnormalities of fibrin formation. These tests are widely available, reproducible, and inexpensive. The PT uses phospholipid brain extracts as a "tissue thromboplastin." The extrinsic pathway is measured by using electrostatically-bound fibrin polymer as an end-point. The PTT uses modified brain lipid as a trigger of the intrinsic clotting system, with fibrin again as the endpoint (Fig 1). These two studies should identify coagulation factor deficiencies if the level of the deficient factor is less than 20 to 35% of normal (normal, mean = 100%). With this and other laboratory tests the normal range is arbitrarily considered to be two standard deviations above and below the mean of the population. This range places 2.27% of normal individuals with results beyond two standard deviations. Values minimally beyond

the normal range may therefore represent either healthy individuals at the extremes of the normal range or those with mild hemostatic defects. This confusion will often affect the interpretation of coagulation studies.

Trauma. Trauma as a cause of bleeding is identified by a clinical examination. If the bleeding is proportional to the degree of trauma, the patient may not require the further confirmation of a negative coagulation screen.

Panel of screening tests of hemostasis. A basic panel of screening tests of hemostasis should include the following: a complete blood count and evaluation of the stained blood smear; a platelet count; a standardized bleeding time; and a PT and PTT. These studies are usually available in most clinical laboratories. A reasonable cost estimate for these studies is $40. Depending on the degree of clinical suspicion that a bleeding diathesis exists, additional studies may be indicated when the preliminary screening panel is normal. This will be discussed later in the section on potential pitfalls of the screening panel.

Positive Screening Test

When one of the basic screening tests is abnormal, the next matter to address is how to pursue further the laboratory investigation to establish a specific diagnosis as to the cause of bleeding. The initial clinical examination and the screening studies may be effectively managed by primary care physicians. However, the further investigation of positive screening tests will often require the input of a hematologist. A detailed description of such investigations is beyond the scope of this article, but a brief outline is provided.

A low platelet count. Bone marrow examination is often required to help differentiate between disorders associated with increased platelet destruction and those that cause decreased production of platelets, especially malignancies. Evaluation of a patient with thrombocytopenia should proceed in consultation with a hematologist.

Prolonged bleeding time. A history of aspirin ingestion should be ruled out. Certain over-the-counter medications such as cough syrups and various pain-relieving compounds contain aspirin; inquiry should be made about their ingestion (Table I). The less likely possibilities of intake of other drugs, or the presence of acquired conditions such as uremia or liver disease, should be considered. If there is no evidence of an acquired disorder or drug ingestion, a congenital platelet dysfunction is the most common cause of a prolonged bleeding time.

von Willebrand's disease is the most common congenital disorder that prolongs the bleeding time. The clotting deficiency is primarily one of VIII/vWF that is synthesized by a autosomal dominant gene. The deficiency of VIII/vWF, however, impairs the functional activity of coagulant factor VIII (factor VIII:C). This results in deficiency of both platelet adhesion (due to decreased factor VIII/vWF) and of fibrin formation (due to decreased factor VIII:C). The deficiency of factor VIII/vWF would be expected to prolong the bleeding time and the deficiency of fibrin formation would prolong the PTT. However, von Willebrand's disease can be extremely variable in its presentation and an isolated abnormality of the bleeding time is common.[12-14]

The diagnosis of von Willebrand's disease is based on specific assays reflecting low levels of the components of the factor VIII complex, including VIII:C, ristocetin cofactor related activity of factor VIII (VIIIR:RCo), and factor VIII-related antigen (VIIIR:Ag). Factor VIII:C is measured by a direct clotting assay. Factor VIIIR:RCo closely reflects the in vivo activity of factor VIII/vWF, that cannot be measured directly by a practical, functional assay. In performing the assay of factor VIIIR:RCo, the antibiotic ristocetin serves as a collagen-like surface to which factor VIII/vWF can bind platelets. Factor VIII:Ag is measured by an immunologic (as opposed to a functional) assay that gives a quantitative measure of how much of the autosomal dominant factor VIIIR:Ag/VIIIR:RCo complex is present. These studies may be performed by reference laboratories.

If von Willebrand's disease is ruled out, other inherited platelet dysfunctions should be considered and evaluated with the use of more specific platelet function studies, such as platelet aggregation tests. These should be performed in consultation with a hematologist.

Prolongation of PT, PTT, or both. The pattern of prolongation of these tests should be considered. An isolated prolongation of the PTT suggests a deficiency of factors XII, XI, IX, or VIII. Further evaluation of this situation should include assays of factor VIII and factor IX to rule out von Willebrand's disease, as well as hemophilia caused by a deficiency of factors VIII or IX. The latter two disorders need only be considered in males since their inheritance is sex-linked. An isolated prolongation of the PT suggests factor VII deficiency. Prolongation of both the PT and the PTT suggests an isolated deficiency of factors X, V, II, or fibrinogen as well as the possibility of a multiple factor deficiency as seen in liver disease, vitamin K deficiency, or disseminated intravascular coagulation. Anticoagulant effect due to drugs—including heparin contamination of the blood specimen—viral illnesses or other conditions should also be considered. These possibilities should be evaluated in a specialized hematology laboratory in consultation with a hematologist.

Pitfalls of Screening Tests

The screening panel has a number of pitfalls. A clear understanding of these limitations is necessary to determine when and what additional laboratory studies are required in spite of a normal screening panel. Disorders that the panel of screening tests may fail to identify include von Willebrand's disease, mild coagulation factor deficiencies, factor XIII deficiency, a platelet dysfunction, vascular disorders, and trauma.

von Willebrand's disease. Not only is von Willebrand's disease the most common hereditary bleeding disorder, but it is also the one most easily missed by these screening tests. It can be extremely variable in its severity; abnormal values for coagulation studies on one day may be followed by normal values on another. The PTT and even the bleeding time will often be normal in this disorder.[13,15]

Since von Willebrand's disease is common, it is important to consider performing more sensitive studies if the screening panel is normal, especially when the clinical evaluation suggests the presence of a bleeding diathesis. The post-aspirin bleeding time is more sensitive than the routine bleeding time and is helpful in identifying von Willebrand's disease. An alternative is to directly assay

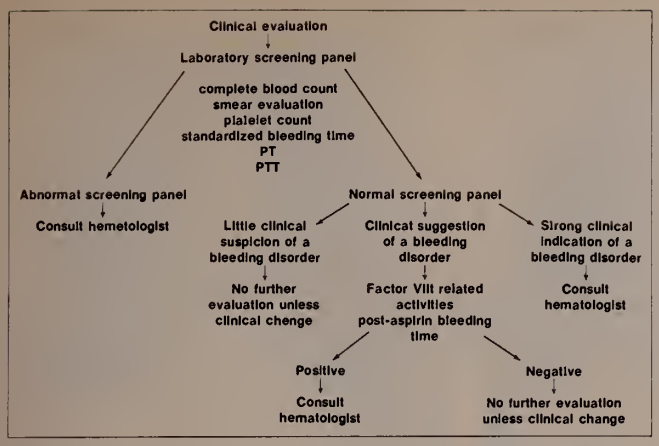

FIGURE 2. Logical schema for algorithm of a child with a possible bleeding disorder. * Evaluation of possible von Willebrand's disease may be initiated by the practitioner with factor VIII related activities assayed in a specialized laboratory.

factors VIII:C, VIIIR:RCo, and VIIIR:Ag. If any of these factor VIII activities border on being abnormal, or if the results are at the lower range of normal (between one and two standard deviations below the mean based on a laboratory's normal ranges), repeat studies are indicated.

Mild coagulation factor deficiencies. As discussed earlier, the limited sensitivity of both the PT and the PTT to detect individual factor deficiencies will cause mild abnormalities to be missed. Except for the possible presence of von Willebrand's disease, abnormalities of this mild degree are usually not clinically significant. Mild qualitative abnormalities of fibrinogen may also be missed, but isolated disorders of fibrinogen are rare. Carriers of congenital disorders such as hemophilia will usually be missed if one relies solely on these screening tests.

Factor XIII deficiency. The end point of both the PT and PTT is the formation of electrostatically-bound fibrin. In the absence of factor XIII covalent bonds will not form in fibrin. Although bleeding may occur clinically, the PT and PTT will be normal. Identification of this rare disorder requires observing the solubility of the fibrin clot in urea. If factor XIII allows covalent bonds to form, the fibrin clot will not dissolve. The test for solubility of fibrin clot in urea is simple, but because of the rarity of the disorder it is usually only performed when the clinical evaluation strongly suggests the presence of a bleeding disorder. A history of umbilical cord bleeding or poor wound healing are suggestive of factor XIII deficiency and indicate that this test should be performed.

Platelet dysfunction. Mild platelet dysfunctions may be missed with the routine bleeding time. As with von Willebrand's disease, the post-aspirin bleeding time will increase the sensitivity of this test and its performance should be considered on the basis of a strong clinical suspicion.

Vascular disorders. As discussed earlier, these disorders are diagnosed on the basis of clinical suspicion. The bleeding time is usually normal.

Trauma. This is obviously a clinical diagnosis.

Further Studies

By understanding the limitations of the screening studies, one may then decide when additional tests are indicated in the face of a normal screening panel. Clinical evaluation and judgment are crucial in making this decision (Fig 2). If suspicion of the presence of an underlying coagulopathy is low based on clinical evidence, further studies are not indicated unless the clinical situation changes. If the evaluation is suggestive of a bleeding disorder, additional studies are aimed at detecting the disorders most likely to have been missed. Specifically, such disorders are most often von Willebrand's disease and the other platelet dysfunctions. The appropriate studies should include a post-aspirin bleeding time, which is useful for both von Willebrand's disease and the other platelet dysfunctions, and an assay of specific factor VIII activities. If the results of these studies do not suggest the presence of an abnormality, further evaluation is probably unnecessary unless the clinical situation changes.

If the clinical evaluation strongly points to an underlying bleeding disorder, other studies are indicated even if the screening panel, post-aspirin bleeding time, and the factor VIII activities are all normal. At this point, the more extensive clinical and laboratory experience of a hematologist is needed to properly choose and interpret the necessary studies.

Experience has demonstrated that accurate clinical assessments will usually identify patients with bleeding disorders who have normal screening panels. The alternative is to do the identical laboratory studies on all persons evaluated. This will result in an excessive number of studies for some patients and too few studies for many others. The rational compromise is to use a basic laboratory screening panel and to modify its use depending on the individual situation. This approach allows the practitioner to initiate the evaluation of these patients and to avoid excessive referrals to a hematologist.

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Superior vena cava syndrome secondary to cervical cancer inappropriately treated with cryosurgery

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Current efforts at cervical cancer prevention and detection rely heavily on the concept of cervical intraepithelial neoplasia (CIN) as a precursor lesion to invasive disease. Patients may be screened for these epithelial lesions quickly and inexpensively with a Papanicolaou (Pap) smear. All patients with abnormal Pap smears then undergo colposcopy, and if CIN is found the lesion may be destroyed and development of invasive disease prevented. Surgical excision, laser surgery, and cryosurgery have all been endorsed as effective means of destroying these precursor lesions. However, indiscriminate use of these techniques may be disastrous since none are adequate therapy for invasive cancer.

Typically, cervical cancer remains confined to the pelvis until late in its natural history. Intercurrent medical disease or ureteral obstruction with infection most often leads to death in advanced stages of the disease. However, patients may occasionally develop extensive, distant metastatic disease. Superior vena cava (SVC) syndrome is rarely seen with cervical cancer, but brief and effective palliation may be obtained with radiotherapy if the diagnosis is quickly established.

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Recently a young woman was referred to the State University of New York at Stony Brook with cervical cancer that persisted after radiation therapy. Surgery and extensive chemotherapy were employed. However, the disease progressed despite treatment, and the patient developed SVC syndrome. Radiation therapy successfully provided brief palliation.

CASE REPORT

A 28-year-old woman presented for routine postpartum care six weeks after an uneventful vaginal delivery. Her prenatal course had been entirely benign; no Pap smear was performed. The patient complained of a foul vaginal discharge and spotting and was treated with topical antibiotics. The discharge and spotting persisted despite many attempts at antibiotic therapy. Cryosurgery was performed for presumed cervicitis. The symptoms continued and six months later a dilatation and curettage was performed that revealed squamous cell carcinoma of the cervix. The patient was staged as IB carcinoma of the cervix and was treated with whole pelvic irradiation.

Cancer recurred in the rectovaginal septum within three months of primary therapy and was treated with interstitial implants and chemotherapy. Despite this, the patient developed bilateral inguinal node metastases and was referred to University Hospital at Stony Brook. Examination, intravenous pyelogram, barium enema, and computed tomographic (CT) scan revealed no other metastases. After considerable discussion, resection of the superficial involved nodes was performed and multi-agent chemotherapy instituted.

The patient developed hoarseness, shortness of breath, and headache 14 months later. Chest radiograph that had previously been normal revealed a diffuse bilateral interstitial infiltrate (Fig 1); CT scan showed supraclavicular and mediastinal adenopathy with dilation of the azygous vein. Nuclear medicine dynamic blood pool scan showed SVC obstruction (Fig 2). Examination revealed neither pelvic disease nor palpable cervical, axillary, or supraclavicular adenopathy. The left arm, anterior chest, and left breast were swollen. Bronchoscopy with biopsy confirmed metastatic squamous cell cervical cancer (Figs 3,4).

Prompt institution of external irradiation to the mediastinum and supraclavicular areas led to the complete resolution of hoarseness and respiratory distress, and the swelling subsided. A normal activity level was resumed.

The patient elected to pursue alternate therapy including mega-dose vitamin therapy and insulin shock treatments. However she died three months later of recurrent, rapidly progressive respiratory distress.

DISCUSSION

Published standards of obstetric care specify the need for cervical cytology on the first prenatal visit.[1] Obtaining a Pap smear presents no hazard to the pregnancy and may detect occult premalignant or malignant cervical disease. Colposcopy may then be performed, diagnosis made, and appropriate therapy instituted. Premalignant lesions may be followed until the successful completion of the pregnancy at which time colposcopy may be repeated and management planned. If invasive

FIGURE 1. Postpartum chest radiograph is entirely normal (left). Chest radiograph fourteen months after initial presentation (right) demonstrates diffuse nodular infiltrates and a wide right paratracheal stripe, consistent with pulmonary metastases and superior vena cava obstruction (or adenopathy), respectively.

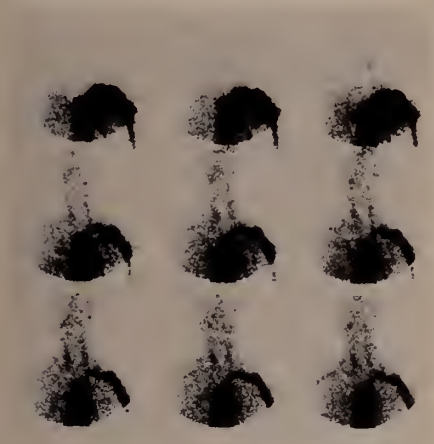

FIGURE 2. A nuclear medicine dynamic blood pool scan demonstrates superior vena cava obstruction with collateral venous flow.

disease is found, the extent of disease can be determined and appropriate surgery or radiation implemented. If a question of possible invasive cancer exists, and cannot be resolved with repeat colposcopic examination, then conization may be performed. This patient did not have the benefit of prenatal cervical cytology and was treated for cervicitis without cytologic or histologic evaluation of the cervix. Cryotherapy is benign in the sense that it is an outpatient procedure requiring no anesthesia and associated with minimal side effects. However, cryotherapy is deadly if misued in patients with cervical cancer.

Townsend and associates reviewed 66 cases of invasive cervical cancer following outpatient evaluation and treatment for cervical disease, and found that 21 patients had been treated for cervicitis, with Pap smears that were either normal or class II.[2] These researchers state that the work-up required prior to treatment of cervicitis should be at least a Pap smear with aspiration of the cervical os, an ectocervical scrape, and colposcopy prior to therapy. The patient reported on here had none of these diagnostic studies performed.

Cryosurgery should not be used to treat cervicitis until preneoplastic and malignant disease of the cervix have been excluded. This requires repeated negative cytologic examinations, and colposcopic evaluation that reveals a normal squamo-columnar junction. No patient should go through pregnancy without the benefit of a Pap smear early in her course. Any cytologic abnormality detected in a pregnant patient must be treated exactly as it would in a nonpregnant woman, with colposcopic evaluation by an experienced examiner.

The natural history of cervical cancer is such that it remains confined to the pelvis until late in its course. The primary lesion extends into the uterine fundus, upper vagina, and adjacent parametrium. Primary lymphatic metastasis is to parametrial and pelvic lymph nodes, and then sequentially to paraaortic nodes. Ureteral obstruction occurs secondary to direct tumor extension in the paracervical region, or to common iliac node enlargement from metastasis. Infection behind the obstructed ureter or renal failure leads to death if intercurrent medical disease does not supervene.

In the patient described earlier, pelvic irradiation apparently controlled central pelvic disease. Lymph node metastasis was first noted in the groin, where tumor seeded from either the rectovaginal septum recurrence or retrograde from pelvic nodal disease. Local control was accomplished by resecting the groin nodes, and chemotherapy was initiated for systemic disease. Lymphatic metastasis to mediastinal and supraclavicular lymph nodes was evidenced by the onset of the SVC syndrome.

The only other reported case of SVC syndrome secondary to cervical cancer occurred in a patient on chemotherapy for nodular pulmonary recurrence. Prompt mediastinal irradiation provided rapid palliation and prolonged survival.[3]

This case presentation emphasizes the tragic consequences of inappropriate use of outpatient cryosurgery, and additionally points out that prompt diagnosis of the SVC syndrome, which is rarely seen with cervical cancer, may allow the prompt institution of palliative radiation therapy.

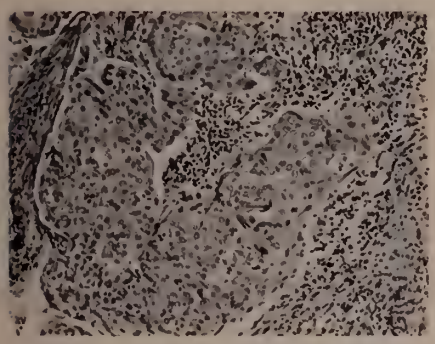

FIGURE 3. Cervical biopsy from patient's primary lesion prior to therapy. (H and E stain; original magnification × 160)

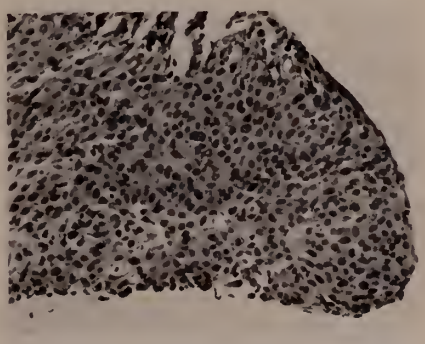

FIGURE 4. Transbronchial biopsy revealing tumor identical to prior cervical lesion. (H and E stain; original magnification × 250)

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Obturator hernia

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Obturator hernia is difficult to diagnose because of its subtle clinical presentation and from a lack of general knowledge and experience with the condition. The clinical manifestations are so vague that for every case diagnosed, there must be many others that are either not recognized or are treated for years with analgesics.

Pierre Roland Arnaud de Ronsil first described obturator hernia before the Royal Academy of Sciences of Paris in 1724. In 1848, Hilton operated on a patient with intestinal obstruction and found a strangulated obturator hernia. He repaired the hernia, but the patient did not survive. The first successful operation was performed by Henry Obre in 1851. A search of the literature reveals that less than 550 cases of obturator hernia have been reported.[1] As the diagnosis remains elusive, the authors report on two cases that exemplify many of the problems; this will perhaps help to keep this rare hernia in focus.

CASE REPORTS

Case 1. A 92-year-old woman was admitted to the Bronx-Lebanon Hospital Center with a diagnosis of congestive cardiac failure. Her medical history revealed atherosclerotic heart disease, mitral insufficiency, and bronchial asthma. The toes of the left foot had been amputated for gangrene. On admission to the hospital, the patient had congestive cardiac failure, the abdomen was flat and nontender, and there were no external hernias or abdominal scars noted. Chest radiograph revealed cardiomegaly and a congestive pattern. Appropriate treatment was instituted.

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The patient complained of right lower quadrant pain and constipation 14 days after admission. There was mild lower abdominal tenderness. Bowel sounds were normoactive and the abdomen was mildly distended. A barium enema showed multiple colonic diverticulae. Pelvic sonogram was normal. The patient was thought to be in poor general condition with congestive cardiac failure and ileus secondary to diverticulitis. The right lower quadrant tenderness persisted and following a bout of dark brown vomitus, upper gastrointestinal endoscopy was done that revealed severe esophagitis and mild gastritis. Antacid therapy and nasogastric suction were initiated.

Shortly after the patient's temperature rose to 104°F and a round, tender swelling was felt in the right femoral triangle. This was found to be an abscess that was resolved by incision and drainage. Intravenous ampicillin was started. Two days later, the abscess site began to drain fecaloid material. The possibility of enterocutaneous fistula due to either femoral or obturator hernia was considered. However, due to the poor general condition of the patient, laparotomy was deferred. Within two days the patient developed brawny edema of the right thigh and leg with blebs and subcutaneous emphysema that required wide drainage and debridement of necrotic muscles and fat. Gram stain revealed enteric organisms. The patient's condition deteriorated and she died 12 days later from multiple organ failure. An autopsy revealed a right obturator hernia of the Richter's type involving the distal ileum and causing partial necrosis of the intestinal wall. This led to an enterocutaneous fistula through the right obturator canal (Fig 1). There was no intraperitoneal contamination.

Case 2. A 55-year-old woman was admitted to the Bronx-Lebanon Hospital Center with a history of colicky abdominal pain, vomiting, and constipation for two days. Her medical history revealed arthritis of the right hip, bronchial asthma, and chronic liver disease diagnosed in 1974. Since she had eight previous admissions for bronchial asthma and abdominal and right hip pain, the patient was considered to perhaps be a complainer. Her first complaint of hip pain dated back to 1974 when she was told that she had osteoarthritis. A barium enema was done at that time because of constipation. A cecal and terminal ileal diverticulum were reported. In 1982 during a hospital admission for abdominal pain the patient also complained of right hip pain. Diagnosis of obturator hernia was considered; however, it was discounted because the Howship-Romberg sign was negative.

Physical examination revealed a woman in moderate respiratory distress. The abdomen was mildly distended with diffuse abdominal tenderness in the right lower and upper quadrants. Abdominal films showed a nonspecific gas pattern. Treatment for asthma and small bowel obstruction was initiated. Despite Cantor tube decompression, the patient's condition did not improve and an exploratory laparotomy was performed. A strangulated right obturator hernia was found. Since it was impossible to release the knuckle of ileum caught in the obturator canal without perforating the bowel, the segment encompassing the hernia was resected and an end-to-end anastomosis performed (Fig 2). The obturator canal was closed with three 0-silk sutures. The postoperative

FIGURE 1. Segment of ileum with a probe marking the fistula on the antimesenteric wall leading into an abscess cavity and muscles of the thigh.

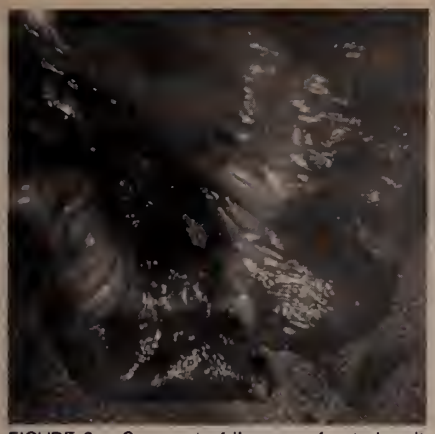

FIGURE 2. Segment of ileum perforated as it was removed from the strangulating obturator canal.

course was uneventful and the patient has had no further right hip pain.

Discussion

Obturator hernia is extremely uncommon before 50 years of age. The female to male ratio is about 6:1.[2] In female patients, the herniation on the right is twice as common as on the left. In male patients, left sided hernia is more common. The usual patient is an elderly, frail woman in the 7th or 8th decade, with a history of multiple pregnancies and recent weight loss. Frequent coughing due to pulmonary disease may propel a loop of small intestine into the obturator canal. Martin and Welch, reporting the largest series, noted a high incidence of obturator hernia in thin, malnourished women weighing 80 to 90 lbs with associated pulmonary disease.[3] In most cases, the sac contains ileum; however, omentum, fallopian tubes, appendix, and Meckel's diverticulum have also been found.[2] In 85 to 90% of cases, the patient presents with gastrointestinal obstructive symptoms. The Howship-Romberg sign—characterized by pain along the obturator nerve that is distributed to the inner side of the thigh and radiating to the knee—is positive in 48% of cases.[2] About 35% of patients give a history of similar pain in the past, as in the second case reported here. Approximately 10 to 20% of patients may have a palpable mass on vaginal examination. Few patients develop enterocutaneous fistulas through the obturator canal, as occurred in the first case. Kozlowski and Beal reported a patient who initially had cellulitis in the right groin that was followed five days later by drainage of fecal material and an intestinal-cutaneous fistula.[4]

Subcutaneous emphysema of the leg as a complication of gastrointestinal disorders is rare. Only two such cases due to obturator hernia have been reported.[5,6] The first patient described in this report had subcutaneous emphysema and is the third reported case in the literature.

Diagnosis of obturator hernia is rarely made prior to laparotomy.[1,2] The usual preoperative diagnosis is intestinal obstruction. The following are four signs of obturator hernia in order of frequency: intestinal obstruction, Howship-Romberg sign, a history of previous similar attacks, and a palpable mass on vaginal examination. The most frequent combination of intestinal obstruction and positive Howship-Romberg sign is present in fewer than one half of the patients. About one third are diagnosed preoperatively on the basis of the Howship-Romberg sign. The Howship-Romberg sign is considered pathognomonic of obturator herniation and correct diagnosis in its absence is improbable. If the Howship-Romberg sign is present, obturator hernia should be suspected immediately. A gas shadow in the region of the obturator foramen is diagnostic on plain abdominal radiographs.[3]

Hannington-Kiff described the absence of the adductor reflex as a worthwhile diagnostic clinical test for obturator hernia. In his two cases, the adductor reflex was absent preoperatively; in the surviving patient, the reflex became positive postoperatively. This test has value even when the Howship-Romberg sign is negative.[7]

The role of the computed axial tomographic (CAT) scan in making an early diagnosis should be given serious and timely consideration. If incarceration is present, a CAT scan of the pelvis and thigh may show the hernia sac between the obturator externus and the pectineus muscle; this should aid in prompt surgical intervention and reduction in morbidity and mortality.[9,10]

Several approaches to repair of the obturator hernia have been suggested. The abdominal approach is the best for establishing the diagnosis and exposing the obturator ring; it is also the least dangerous to the obturator vessels and permits resection where necessary. The retropubic approach was advocated by Cheatle and Henry.[11] However, this method is useful only when a correct preoperative diagnosis is made. The obturator approach is recommended when a palpable hernia is present. A generous vertical or oblique thigh incision is required; the adductor longus is retracted medially and the pectineus muscle laterally to expose the hernia sac.

In most cases, it is sufficient to invert the sac, ligate the neck, and excise the sac. It is commonly felt that simple reduction of the hernia sac is not sufficient and recurrences have been reported.[2] The defect is usually closed with interrupted silk sutures. At times it may be necessary to use a flap of pectineus muscle, rib cartilage, Teflon cloth,[11] or Marlex mesh[12] to bridge defects.

The mortality rate for obturator hernia varies from 50% to 10% in different series. In view of the advanced age and poor nutritional status of the patients, the infrequency of accurate preoperative diagnosis, and the delay in treatment, this operative mortality should be considered high but acceptable. Alertness to the varied presentations, clinical awareness, and early CAT scan should be employed to reduce the mortality of this intriguing hernia.

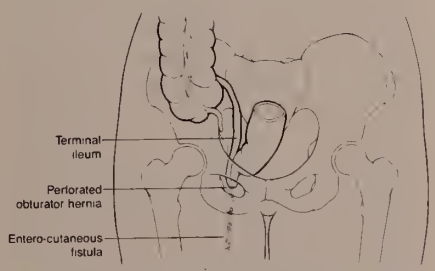

FIGURE 3. Line drawing showing herniation through the obturator canal with strangulation and resultant fistula drainage through the thigh.

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Radiation therapy associated cancer of the esophagus

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Several factors have been associated with an increased incidence of esophageal carcinoma: alcohol consumption (particularly if brewed with maize); tobacco use (especially chewing); nitrosamines; vitamin deficiencies; Plummer-Vinson syndrome; familial tylosis; achalasia; and strictures.[1] Radiation has been shown to induce esophageal carcinoma in mice at very high doses (>11,000 rad).[2] In persons irradiated in the Japanese atomic bomb explosions, an increased incidence of esophageal cancer was seen in Hiroshima where heavy neutron fall-out occurred but not in Nagasaki.[3] Several cases of esophageal cancer following therapeutic radiation have also been reported.

CASE REPORT

A 71-year-old woman presented in June 1982 with an eight month history of progressive dysphagia and weight loss. An esophagram and endoscopy revealed a large obstructing polypoid lesion in the cervical esophagus. The patient had no evidence of distant metastasis. The anterior lower neck showed mild fibrotic changes and moderate telangiectasia. Endoscopic biopsy showed a moderately well-differentiated squamous cell carcinoma.

The patient had a history of thyrotoxicosis in 1935 that was treated with iodine and twice with partial thyroidectomy. With persistent hyperthyroid symptoms, she began radiotherapy to the thyroid in 1938. Treatment consisted of a 200 rad surface dose every three weeks for seven treatments using a 100-Kv, 3 mm HVL superficial therapy unit with 3 mm AL filtration.

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The patient's symptoms improved with reduction in her estimated basal metabolic rate and her exophthalmos. Telangiectasia in the treatment area was first noticed in 1940.

The patient received an additional 1,000 rad in 1941 and 800 rad in 1942 for recurrent symptoms. The total dose was 3,200 rad given over a four year period. Based on her current anatomy, the dose to her esophagus is estimated to have been between 930 and 1,390 rad.

In 1952, the patient began thyroid replacement therapy (subsequent ^{131}I scans showed heterogeneous uptake thought to be secondary to radiation fibrosis). Because of her age, cardiac disease, and tumor location, the esophageal carcinoma was not treated surgically. She began chemotherapy in August 1982, with cisplatin and vinblastine. Because of leukopenia and persistent obstruction, chemotherapy was discontinued and she began radiotherapy in September 1982. She received 2,400 rad tumor dose in three weeks via two anterior oblique portals with partial improvement in her obstruction. The patient died at home one year later from tumor progression.

DISCUSSION

Radiation-induced cancer of the esophagus appears to be rare. With neutron-photon irradiation, the incidence in Hiroshima survivors increased four-fold with doses above 200 rad but did not increase at any dose in Nagasaki where much less neutron fall-out occurred.[3] In 1949, Quimby surveyed more than 100 radiologists and thyroid specialists to ascertain the incidence of radiation cancer following thyroid irradiation. One case of esophageal carcinoma was reported.[4] Since then, an additional 22 cases of esophageal carcinoma occurring in previously irradiated areas after a minimum latent period of five years have been reported.[4-11]

The true incidence of esophageal carcinoma developing in irradiated patients cannot be estimated accurately since all persons developing the cancer are unlikely to have been reported, and the total number irradiated may also not be accurately assessed. The current case is the only radiation-associated esophageal cancer reported at this medical center. Assuming that other cases were not lost to other hospitals, the incidence of esophageal carcinoma associated with irradiation for thyrotoxicosis, as well as for other reasons, is less than 0.5%. This is not higher than the naturally occurring esophageal cancer rate.[12]

It does not appear that the risk of esophageal radiation carcinoma is high enough to warrant special screening procedures or to effect decisions for cancer therapy. However, there does appear to be a small increased risk—even after very long latent periods and relatively low doses—that merits increased awareness by physicians and previously irradiated patients so that early presentation and work-up of esophageal symptoms may be undertaken.

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Pachydermoperiostosis: a paraneoplastic syndrome

C. Ronald MacKenzie, MD

Pachydermoperiostosis is a clinical syndrome characterized by clubbing of the digits, periosteal new bone formation, and soft tissue changes involving the scalp (cutis verticis gyrata).[1-3] The majority of reported cases have been clustered within families or were idiopathic. Due to its resemblance to hypertrophic osteoarthropathy, pachydermoperiostosis is classified as a primary form of this better known disorder.[1-3] Though extremely rare, pachydermoperiostosis has been reported to develop as an accompaniment to malignancy.[4,5] The following report is of a man who developed the syndrome in the setting of acute myelomonocytic leukemia.

Case Report

A previously well 60-year-old man presented in the fall of 1979 with a ill-defined, musculoskeletal syndrome. It consisted of right flank and groin pain that progressed to include neck stiffness with pain radiating to both shoulders and rendering him bedridden. He was admitted to the hospital for further investigation in February 1980. The physical examination was normal except for fever (38.7°C), generalized discomfort, and a limited range of motion in the spine associated with impaired straight leg raising. Laboratory investigation revealed anemia (hematocrit, 30.8%) with a reticulocyte count of 1%, and leukopenia (white blood cell count, 2,800/mm); there were 70% lymphocytes, 20% polymorphonuclears, 7% monocytes, and 1 to 2% eosinophils. The platelet count was normal and the sedimentation rate was 89 mm/h. A preleukemic state was suspected and confirmed with bone marrow biopsy. No specific cause for his musculoskeletal symptoms was found, and a tentative diagnosis of polymyalgia rheumatica was made. Corticosteroid treatment resulted in a marked symptomatic improvement but produced no change in the hematologic abnormalities.

The patient was readmitted because of abdominal pain and hepatomegaly 16 months after initial onset. Repeat bone marrow biopsy revealed an increase in cellularity and in the number of blasts consistent with an evolving myelomonocytic leukemia. Liver biopsy demonstrated extramedullary hematopoiesis and nonspecific reactive changes.

In October 1981 a blood count revealed circulating blast forms; bone marrow examination confirmed the diagnosis of acute myelomonocytic leukemia. Physical examination revealed several new and unusual features. Inspection of the head demonstrated large folds and deep furrows over the vertex of the scalp; these could not be obliterated by stretching (Fig). This—the typical picture of cutis verticis gyrata—extended anteriorly to involve the frontal region. In addition, deep nasal grooves and loose redundant eyelids were present. The patient had not been aware of these abnormalities nor had they been documented on previous examinations. He was unaware of similar changes in any family member (one brother) though none were alive to verify this impression. The fingers and, to a lesser extent, the toes showed mild but typical clubbing.

Laboratory investigation was consistent with acute leukemia. Serum growth hormone and somatomedin levels were normal. Radiographic examination demonstrated periosteal new bone formation distally over the femora. Technetium bone scanning revealed asymmetric uptake in the mid and lower aspects of the right femur. The admis-

FIGURE. Photograph of the scalp demonstrating the large folds and furrows of cutis verticis gyrata.

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sion chest film was normal. Induction chemotherapy was instituted and later repeated because of focal persistence of leukemic cells. Severe marrow aplasia accompanied by multiple complications ensued; despite intensive supportive measures, the patient died due to polymicrobial sepsis.

Post mortem examination revealed marked jaundice and multiple petechiae and ecchymoses over the trunk and extremities. On gross inspection of the head, the previously described scalp changes persisted unchanged as did the digital clubbing. On microscopic examination the scalp demonstrated an increase in the dermal fibrous and elastic tissue, dilated lymphatic channels, and a predominantly perivascular nonspecific infiltrate. The lungs were diffusely hemorrhagic and contained fungal hyphae consistent with *Aspergillus* species. The pleural surfaces appeared normal and lung carcinoma was not found. Samples from bone marrow sites demonstrated marked hypocellularity, and sections of the distal femora revealed periosteal new bone formation. No foci of residual leukemic cells were found in any tissue, including the scalp and the femoral periosteum.

Discussion

The inability to obliterate scalp folds is considered diagnostic of cutis verticis gyrata.[1,2] The microscopic appearance of the scalp with the normal epidermis and the increase in fibrous and elastic elements is consistent with previous reports.[2] Cutis verticis gyrata and digital clubbing—both classic features of pachydermoperiostosis—were the striking clinical findings in the patient presented here. Although such phenomena have been reported as consequences of leukemic infiltration, the changes characteristically resolve with therapy.[6,7] In this patient, both anomalies persisted unchanged. Marrow samples and biopsies of the femora and scalp failed to reveal the presence of leukemic infiltrates. However, periosteal new bone formation was demonstrated in the distal femora. Except for the terminal fungal pneumonia, there was no evidence of pre-existing lung or pleural disease that could have independently accounted for this picture. The negative family history, the absence of prior documentation of the skin lesions, and the patient's conviction that these phenomena were of recent onset all argue that they were late, secondary events.

From a clinical standpoint, three major syndromes with overlapping features constitute the hypertrophic osteoarthropathies: simple clubbing of the digits, pachydermoperiostosis, and secondary hypertrophic osteoarthropathy.[1,3] These syndromes have been known for centuries in the form of clubbing. Classic descriptions of pachydermoperiostosis appeared in the literature in the late 19th century, though early clinicians confused this disorder with acromegaly or the newly described pulmonary hypertrophic osteoarthropathy. The syndrome was not defined until 1935 when Touraine, Solente, and Gole recognized the association between the skeletal manifestations of hypertrophic osteoarthropathy and the scalp lesion of cutis verticis gyrata.[1-3]

Pachydermoperiostosis is a self-limited disorder. Beginning in adolescence, patients observe the insidious onset of clubbing and enlargement of the distal extremities. Nonspecific rheumatic complaints and hyperhidrosis of the hands and feet may accompany these physical changes. The cause of the disorder remains obscure. Some cases appear familial although the precise mode of inheritance is unknown. Examples of affected siblings with normal parents as well as those of consanguineous parentage suggest heterogeneity or recessive inheritance.[8] From an analysis of 78 cases, however, Rimoin concluded that an autosomal dominant inheritance with marked variability in expression best explained the genetics of the disorder.[9] Further, pachydermoperiostosis may occur in the absence of a positive family history; in these patients no definitive chromosomal abnormality has been detected.[10] Such cases are considered idiopathic. There are also rare reports in which physical changes indistinguishable from pachydermoperiostosis have developed in association with malignancy.[4,5] In such cases the syndrome apparently arises as a remote effect of the neoplasm.

In contrast, secondary hypertrophic osteoarthropathy always occurs as a result of another disease.[1,3] Classically the triad of clubbing, periosteal new bone formation, and arthritis arises in the setting of bronchogenic carcinoma. However, it has been reported to occur in numerous other diseases.[13] Several features including a later age of onset, a more rapid evolution of signs and symptoms, and usually the absence of associated skin changes distinguish this syndrome from the primary disorder. It has been observed, however, that facial and scalp changes similar to those of pachydermoperiostosis may occur with the secondary syndrome,[1] making precise classification difficult in such cases.

Several skin disorders, including acanthosis nigricans[4] and scleroderma-like changes in the hands and feet[11] have been associated with hypertrophic osteoarthropathy. Cutis verticis gyrata, an entity not well known to internists, is the most common. Polan and Butterworth, in their review of 275 cases, found that one half accompanied local conditions of the scalp or a systemic disease.[12] Of the latter, acromegaly was the most common. Although one case of leukemia was listed in this survey, an examination of the report has raised doubts about the hematologic diagnosis.[6] The remaining cases were considered idiopathic.

Thus, on both clinical and pathologic grounds, the patient presented here had developed a syndrome resembling pachydermoperiostosis in the setting of myelomonocytic leukemia. There was no evidence to suggest that the physical characteristics antedated the terminal illness. There was also no apparent family history of the disorder. Conditions that might mimic or independently produce the syndrome were not found. Scattered case reports have documented the occurrence of similar phenomenon in the setting of malignancy. However, they have not yet been reported as a consequence of leukemia.

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Appendiceal diverticulum: an unusual but not uncommon entity

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Although more than 1,400 cases of appendiceal diverticular disease have been reported in the literature,[1-11] a recent edition of a major surgical text[12] fails to mention the entity. Although individual series have generally been small, enough experience has been accumulated that a characteristic presentation may be described. In this article, the experience with appendiceal diverticula at the Mount Sinai Hospital for the past 15 years is discussed and compared with other published reports.

CASE REPORT

A 54-year-old woman came to the emergency room complaining of burning abdominal pain radiating to the right groin and lower back, nausea, vomiting, diarrhea, chills, and fever for three days. She also reported weakness and malaise for almost three weeks. The patient had peptic ulcer disease two years earlier that was treated medically and without recurrent symptoms.

On physical examination she was afebrile with abdominal distention and tenderness in the lower abdomen, especially on the right. Pelvic and rectal examinations were normal. The white blood cell count was 9,900/mm; electrolytes, liver function tests, and amylase were normal. Abdominal radiographs were remarkable for several dilated loops in the mid abdomen with air/fluid levels. A sonogram was performed and failed to reveal any intra-abdominal abnormality because of the dilated intestine. The patient was admitted to the hospital and treated with intravenous fluids and cefazolin.

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In the hospital the patient remained afebrile, and her abdominal examination revealed less tenderness and distention over the next two days. A barium enema on the third hospital day showed an extrinsic mass compressing the medial aspect of the cecum and no filling of the appendix, consistent with an appendiceal abscess. On the fourth hospital day, her temperature rose to 38.2°C, and she developed increased tenderness in the right lower quadrant. In view of the deterioration of the patient's condition an exploratory laparotomy was performed. A perforated appendix with a localized paracecal abscess was found. The terminal ileum was adherent to and formed part of the wall of the abscess cavity. Appendectomy and drainage were performed. The patient was given intravenous clindamycin and tobramycin for eight days and her course was uneventful. The pathologic report revealed acute and chronic diverticulitis of the appendix (Fig).

A review of cases from 1969 to 1983 at this institution revealed six additional cases of appendiceal diverticula (Table). In four of five cases, including the one described here, a laparotomy for treatment of a right lower quadrant inflammatory process was delayed from seven to ten days due to the unclear nature of the patient's complaint. The average age of the five patients for whom nonincidental appendectomy was performed was 47.2 years. Associated acute appendicitis was seen in three of the five cases of patients with appendiceal pathology.

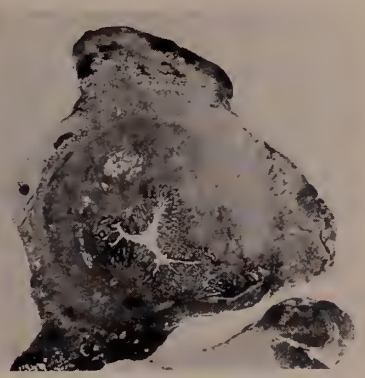

FIGURE. Appendiceal diverticulitis (note the absence of muscular layers beneath the mucosa).

DISCUSSION

The overwhelming majority (97% of the cases in a collective review by Trollope and Lindenaur)[1] of appendiceal diverticula are false or pseudodiverticula (absent muscularis propria) on histologic section. Less than 50 cases of true diverticula (containing all layers of the intestinal wall) have been reported. The incidence of appendiceal diverticula has varied in the literature from 0.004 to 2.1%. To some extent the incidence of appendiceal diverticula in any series will be a function of how willing the surgical pathologist is to search for this entity.

An appendiceal diverticulum may present in the following ways: with or without inflammation of the diverticulum; with or without associated appendicitis; or incidently.[1,10] When acute inflammation exists as in the first two instances, clinical assessment may help differentiate between appendiceal diverticulitis and acute appendicitis. However, the index of suspicion for appendiceal diverticulitis is usually low before surgery.

Patients with appendiceal diverticulitis tend to present with prolonged, in-

TABLE. Review of Cases From 1969 to 1983

Patient	Age/ Sex	Presentation	Clinical diagnosis	Pathologic diagnosis
1	47/M	14 days right lower quadrant pain; 3 days, second episode right lower quadrant pain	Acute appendicitis with localized perforation and abscess	Appendix with diverticulosis and diverticulitis; fistulous tract
2	15/M	30 days hospitalized for appendiceal abscess; one day second episode	Acute appendicitis	Acute appendicitis and periappendiceal abscess, with origin of inflammation in a diverticulum
3	36/M	Ten days umbilical and right lower quadrant pain	Acute appendicitis with periappendiceal abscess	Chronic, acute appendicitis; periappendicitis with diverticulitis
4	55/F	Incidental	Normal appendix	Appendix with diverticulum
5	75/M	Incidental	Normal appendix	Appendix with diverticulum
6	84/M	One day epigastric and right lower quadrant pain	Acute appendicitis	Acute phlegmonous appendicitis; severe periappendicitis with a diverticulum and a tubulovillous adenoma at the tip
7	54/F	Seven days lower abdominal pain, more on right	Periappendiceal abscess	Appendix with acute and chronic diverticulitis with perforation; serosa with acute, chronic inflammation

dolent, ill defined abdominal pain[10] that is usually confusing to the clinician. This is, however, not always the case and a picture of acute appendicitis may predominate.[7,8,11] The average age of a patient with appendiceal diverticulitis is older than the patient with acute appendicitis—the third versus the fifth decade[10]—and there is a tendency for patients to present with recurrent attacks of pain prior to definitive surgery.[11]

The pathogenesis of appendiceal diverticula is not certain, although several theories exist: postinflammatory weakness; congenital or perivascular weak spots (similar to theories of colonic diverticulum formation); excessive muscular contraction; and increase in intraluminal pressure secondary to obstruction or traction.

The clinical importance of the entity lies in its recognition. When one is dealing with a patient with abdominal pain of somewhat obscure cause and prolonged course, this clinical condition should be considered. Enough cases have now been reported that appendiceal diverticulitis, while unusual, should at least be considered in the differential diagnosis of right lower quadrant pain.

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This section is designed to offer rapid publication (usually within 1–3 months) of new clinical, epidemiologic, and laboratory observations, as well as of comments on articles published in the Journal *or on any topic related to the role of the physician. Letters should be typed double-spaced and should include the professional affiliation, highest academic degree, address, and signature of each author. Preference is given to letters not exceeding 450 words. All letters are personally reviewed and acknowledged by the Editor. Address correspondence to Editor,* New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042.*

Dementia, myoclonus, and EEG findings typical of Jakob-Creutzfeldt disease in a patient with Alzheimer's disease

TO THE EDITOR: The differentiation between dementia of Alzheimer's type and that secondary to Jakob-Creutzfeldt disease (JCD) is usually straightforward. Patients with JCD, a viral induced transmissible dementia, generally present with a triad of dementia, myoclonus, and characteristic findings on the electroencephalogram (EEG), notably periodic sharp wave complexes.[1,2] Although patients afflicted with Alzheimer's disease, a non-transmissible dementia, may also show myoclonus, these patients do not have pathognomonic EEGs. The EEG in such cases typically demonstrates an increase in electrophysiologic slow wave activity. The following report describes a patient with pathologically confirmed Alzheimer's disease and myoclonus in whom a diagnosis of Jakob-Creutzfeldt disease was entertained due to the presence of periodic sharp waves on EEG.

Case Report. A 62-year-old man, despite previous good health, was afflicted with a progressive dementing illness for eleven years prior to his death. The patient's family sought professional help after two years of increasingly severe memory loss and confusion. The family history was unremarkable. Initial examination revealed poor recent and remote memory, fluent dysphasia, substitution perseveration, and paraphasia. No focal neurologic findings were evident. The EEG findings were nonspecific, revealing only generalized background slowing. A computed tomographic (CT) scan of the brain and pneumoencephalogram indicated both central and cortical atrophy. The presumptive diagnosis at this stage was that of senile dementia of the Alzheimer type.

The patient's subsequent course was marked by gradual deterioration. Within five years of onset, the patient was without intelligible speech, incontinent of urine and feces, and required total body care. Recurrent hospital admissions occurred over the ensuing six years for infectious complications. Increasing spasticity was noted in addition to primary generalized tonic-clonic seizures appearing five years prior to death and controlled with phenytoin. One year prior to death the patient developed asymmetric myoclonic jerking of all four extremities.

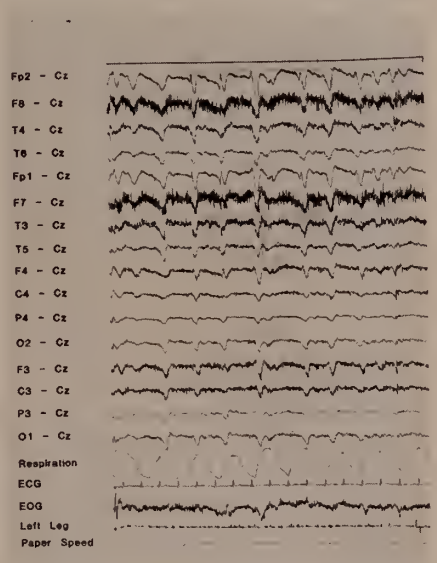

FIGURE 1. Pseudoperiodic generalized triphasic waves with posterior background slowing as demonstrated on EEG.

During the patient's last hospital admission for aspiration pneumonia, an EEG was repeated for increasingly severe myoclonus. As seen in Figure 1, pseudoperiodic generalized triphasic waves with posterior background slowing were demonstrated. The triphasic waves were 250 ms in duration and occurred with a variable periodicity of 0.5 to 1.2 s. Activity was symmetric, bisynchronous, and maximum in the frontal regions.

The postmortem examination revealed an atrophic brain weighing 980 gm with marked ex-vacuo dilatation of the lateral and third ventricles. Microscopic sections of the brain (Fig 2) revealed changes consistent with Alzheimer's disease with neuritic plaques and neurofibrillary tangles occurring diffusely. Granulovacuolar degeneration was also prominent in the hippocampus. Spongiform changes characteristic for Jakob-Creutzfeldt disease were not present.

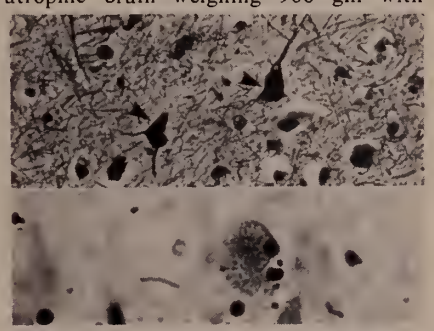

FIGURE 2. Microscopic sections of the brain revealing neuritic plaques (top) and neurofibrillary tangles (bottom) occurring diffusely.

Discussion. The case presented is the third known patient described with Alzheimer's disease manifesting the clinical triad of dementia, myoclonus, and periodic EEG complexes. The periodic discharges, typical of Jakob-Creutzfeldt disease, may occur in both the early and late stages and are generally triphasic and preceded by high voltage rhythmic slow waves.[3] Monophasic, biphasic, and polyphasic short waves have also been reported. Unlike the atypical periodic sharp wave complexes in the two previously reported cases of Alzheimer's disease, the present case demonstrates a periodicity (0.5 to 1.5 s) consistent with such a diagnosis.[4] Periodicity on EEG may also occur in postanoxic states, toxic metabolic encephalopathies, subacute sclerosing panencephalitis, cerebral lipidoses, and postviral and subcortical arteriosclerotic encephalopathies.[3,5] Although preterminal postanoxic changes might be implicated as the cause of the EEG changes in the patient reported here, the long duration of the myoclonic activity and its association with the periodic sharp wave complexes as described makes such an explanation less likely.

The late onset of myoclonus and periodic sharp wave complexes on EEG, although atypical for JCD, is not inconsistent with such a diagnosis. In fact, transmissible dementia may appear at any time in the setting of a degenerative brain disorder such as Alzheimer's disease. Traub and associates describe several patients thought to have a central nervous system pathology distinct from JCD but who subsequently developed features typical for a spongiform encephalopathy up to several years following disease onset.[6]

The myoclonus found in both Alzheimer's and Jakob-Creutzfeldt disease is not distinctive; differentiation by means of location and symmetry of the myoclonic activity, age at onset, or temporal profile of the underlying dementia is generally unrewarding. Myoclonus in Alzheimer's disease is common, exceeding 50% in some series and occurring with equal frequency in both males and females.[7-10]

As this patient demonstrates, differentiation between JCD and Alzheimer's disease may at times be difficult. Accurate diagnosis antemortem is important, however, to insure proper handling of body fluids and tissues. Although the risk of infection does not appear to be increased among medical personnel who come into contact with patients afflicted with JCD, prudence dictates simple precautionary measures.[11] Exposure to saliva, urine, or feces requires simple hand washing whereas percutaneous exposure to blood or cerebrospinal fluid warrants cleansing with 0.5% sodium hypoclorite. Instruments contacting blood or tissue should be autoclaved for one hour at temperatures exceeding 121°C or treated with concentrated sodium hypochlorite.[12-14]

In conclusion, this case illustrates a rather unusual presentation of Alzheimer's disease and the difficulty in differentiating such cases from Jakob-Creutzfeldt disease. The potential for infectivity in JCD demands an appreciation for and knowledge of such overlapping signs and symptoms.

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AIDS in the wife of a bisexual man

TO THE EDITOR: The acquired immunodeficiency syndrome (AIDS) is a disorder of the cell-mediated immune system caused by human T lymphotrophic virus type III (HTLV-III), and is manifested by life threatening opportunistic infections or Kaposi's sarcoma. What had begun as a curosity among homosexual men in New York City, Los Angeles, and San Francisco[1] has now become a major epidemic in the United States.[2] In general, the disease has been limited to homosexual or bisexual males, intravenous drug abusers, patients with hemophilia, and blood transfusion recipients. However, it has recently been reported that sexual contacts of either patients with AIDS or those in high risk groups for AIDS have the potential for developing AIDS.[3] This is of concern in that a universally fatal disease has the potential to spread outside its original boundaries into the larger heterosexual community. What makes this prospect so unsettling is that the disease may be acquired from sexual partners who have been exposed to HTLV-III but who are not themselves symptomatic.

Case Report. We recently treated a 33-year-old woman with AIDS who apparently acquired the disease from her bisexual husband who showed no manifestations of the disease. This patient had no history of drug abuse, steroid or immunosuppressive therapy, or evidence of hematologic malignancy. She had never received a blood transfusion, and while she maintained regular sexual relations with her husband, she denied any extramarital sexual contacts during their 12-year marriage. She was born in the United States and has lived here her entire life.

This patient presented with a few months history of fever, weight loss, cough, and shortness of breath. On physical examination she was tachypneic at a rate of 30/min. Examination of the pharynx revealed oral candidiasis. There were rales in both lung fields. A chest radiogram showed bilateral interstitial infiltrates. A transbronchial lung biopsy was performed and methenamine silver stains were positive for *Pneumocystis carinii*. She was successfully treated with pentamidine isothianate due to intolerance to trimethoprim sulfamethoxazole.

The patient's husband is a 37-year-old man who for the last five years has maintained an active bisexual lifestyle in New York City. Except for hepatitis in early 1985, his medical history is not significant. He denied any fever, unexplained weight loss, skin rash, headache, shortness of breath, or diarrhea. He had no risk for AIDS outside of homosexual contacts. On physical examination he had some anterior cervical adenopathy. The pharynx showed no signs of infection, his lungs were clear, and the spleen was not palpable. Regular follow-up examinations have shown no evidence of opportunistic infection or Kaposi's sarcoma.

Discussion. Pneumocystis carinii is a protozoan parasite that typically causes pneumonia in severely immunocompromised hosts. This patient had *Pneumocystis carinii* pneumonia as revealed by biopsy. The presence of this infection with no other disease process that could account for immunosuppression satisfies the Centers for Disease Control case definition of AIDS.[4]

We report this case as another example of the spread of AIDS into the heterosexual community. Unsuspecting carriers of HTLV-III who may or may not develop AIDS may apparently transmit it to others. HTLV-III is fast becoming a ubiquitous virus in certain homosexual and drug addicted communities.[5,6] Intimate sexual or blood contact with these individuals may lead to the development of AIDS. This patient's only apparent means of acquisition of HTLV-III was through sexual contact with her husband. Therefore, we can expect greater numbers of heterosexual contacts not otherwise at risk

for AIDS to develop this disease in the future.

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Pleural effusion and gastric ulcer

TO THE EDITOR: I recently received a letter from Dr Yong-Myun Rho with a reprint of a case report he published 15 years ago.[1] The case is nearly identical to the one my co-authors and I recently published in the *Journal*.[2] It describes a patient with gastric rupture into the left pleural space. Library searches for case reports are only as good as the titles searched and reflective of the inclusive years requested. Although we searched as far back as 1950, we did not uncover Dr Rho's paper.

His paper deserves mention for a number of reasons. Two cases proven by autopsy, his and ours, are more convincing than one that this rare entity exists. The clinical course of the case he described was very similar to ours with profound hemodynamic collapse and respiratory failure. Finally, and most importantly, Dr Rho is a gentleman. In his kind note to me he never said, "I had the first case!"

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Foreign medical graduates

TO THE EDITOR: The article appearing in the October issue of the *Journal* concerning substandard medical education and the government's responsibility to protect the public raises some very interesting thoughts.[1] This controversial issue of patient safety is very often used as an excuse by those in favor of limiting physicians not only in New York State, but throughout the entire country. A projected physician glut within the next decade has suddenly aroused alarming interest as to the qualifications of foreign medical graduates (FMGs) and how they compare with graduates of American medical schools. Was this an issue when the US immigration laws were made very permissive in the 1960s and 1970s?

The Educational Commission for Foreign Medical Graduates (ECFMG) was established for the purpose of evaluating clinical competence as well as basic science knowledge. A qualifying examination was developed assuring training hospitals as well as the public that those achieving a passing grade had met American student standards. FMGs subsequently entered this country, passed the examination, and filled residency positions. Residency positions now cannot accommodate all applicants. So why is it that in the face of a projected physician glut, the ECFMG examination is criticized as being "less difficult and comprehensive than the National Boards" when in fact every question used by the ECFMG on the examination has appeared at least once on the National Boards?[2]

Obviously, the problem lies not with the qualifying examinations themselves, since only 3.8% of the US Foreign Medical Graduates (USFMGs) taking the examination pass. Rather it is with the governing and accrediting process and licensing boards. In these times of a highly litigious society the medical profession needs today, more than ever, compassionate, humane, and communicative teachers who have developed into constructively skeptical thinkers. An offshore medical education may not be what Hippocrates had in mind. However, as a result of learning a new language and adapting to a new and different culture by living within these often poverty-stricken countries, these essential qualities, so often admired in a physician, are incorporated into the attitudes of the highly motivated and dedicated individuals who bravely decide to diligently pursue the only alternative to an American medical education.

Multiple choice examinations cannot evaluate these intangible, essential qualities. The mere passing of an examination has apparently justified medical competence to the licensing boards in this country since the establishment of the National Board and ECFMG examinations. However, until methods are established by either the individual institution or at the national level, those students who are willing to and do comply with the present requirements of passing an examination should not be unjustly punished by being excommunicated from the practice of medicine as poorly-educated "threats to society."

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In reply: I wish to acknowledge Mr Murach's articulate letter. Although we are polarized in our perceptions and conclusions regarding the quality of medical education in the off-shore medical schools, I would like to comment on some of his arguments.

As he indicated, there was a muted response to the large influx of Foreign Medical Graduates (FMGs) in the early 1970s. This was due in part to the unrealized hope that the FMGs would provide greater access to medical care for under-served populations. Unrealized, I say, because longitudinal studies of FMGs have shown that they followed the specialty and geographic distribution of USMGs in a very similar pattern. More pertinent to his and my discussion is the fact that more than one half of the FMGs came from medical schools in Europe and Canada that are either accredited by the US accrediting organization or by a national accrediting body in the European country whose standards are entirely analogous to those of the United States. For-profit schools such as those that characterize off-shore institutions and a number

now in the Philippines were previously nonexistent. US Foreign Medical Graduates (USFMGs) now exceed Alien Foreign Medical Graduates (AFMGs); the majority were educated in substandard off-shore medical schools.

Mr Murach equates the old ECFMG examinations with the National Boards. Quantitatively, the ECFMG examinations contained only about 20% of the questions that are standard in the two day NBME examinations. In fact, the Foreign Medical Graduate Examination in the Medical Sciences (FMGEMS) was a response of the ECFMG to criticism of their earlier examinations. His characterization of the off-shore medical schools is not the same as that described in the advertising brochures. In fact, I was distressed to read in a Project Hope report of a visit to Grenada, where the medical care of the indigenous population was essentially nonexistent, that no mention was made of assistance by the St. George's medical student body. Where were these dedicated individuals?

Mr Murach also describes diligent pursuit as the "only alternative to an American education." The Association of American Medical Colleges (AAMC) has made an analysis of USFMGs of the off-shore schools and reports that less than one half apply to US medical schools. That *is* surprising, isn't it?

I agree with Mr Murach that a multiple choice examination such as even the FMGEMS does not provide assurance of clinical competence nor, even less so, of the intangible qualities of character that he mentions. Only an improved selection process may be helpful for the latter and a clinical examination by interactive computer may provide greater evaluation of clinical competence. This is in the testing phase now.

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CHEMICAL DEPENDENCE

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CONTEMPORARY NEPHROLOGY

Volume 3. Edited by Saulo Klahr, MD, and Shaul G. Massry, MD. 768 pp, illustrated. New York, Plenum Publishing Corp, 1985. $89.50 (hardcover)

Continuing the tradition of excellence established by the previous issues of *Contemporary Nephrology*, this volume represents a comprehensive treatise dealing with most aspects of modern nephrology. The text, spanning over 500 pages of highly sophisticated modern knowledge, is the contribution of 26 authorities in various fields. The 15 chapters smoothly dovetail and in the remaining 200 or so pages one finds, with some repetitions as expected, more than 3,300 representative references summarizing recent conceptual, technologic, and therapeutic ideas.

The reader is reintroduced to the original concepts of H.W. Smith (1937) and R.F. Pitts (1945), brought up into the 1950s and finally to the methodologies of recent years in the realms of membrane transport, renal hemodynamics and metabolism, production and effects of prostaglandins, and acid-base and mineral physiology. A highly clinical essay deals with the identification, evaluation, and treatment of the sodium-sensitive hypertensive individual. An exhaustive chapter precisely dissects the immunologic mechanisms of renal disease. In addition, the importance and meaning of proteinuria and the diagnostic role of kidney biopsy are thoroughly evaluated. Acute renal failure, the effects of microvascular and hemopoietic disease on the kidney, uremia, nutrition and renal disease, quantitation of dialytic therapy, the effects of drugs on the kidney, and the basic and most recent knowledge on renal transplantation close the book in a thorough presentation of "what's new" in these subjects.

Maintaining their original goal "to divulge the major advances in nephrology," the editors have neatly amalgamated this array of information and have produced a tightly packed mixture of up-to-date knowledge, highly useful to those already devoted to or recently initiated in nephrology and allied sciences.

This volume indeed represents a significant contribution to modern nephrology, providing the reader with easy access to a large body of either factual or hypothetical but always extremely stimulating data generated by active work in this progressively expanding discipline. This reviewer highly recommends it.

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UROLITHIASIS AND RELATED CLINICAL RESEARCH

Edited by Paul O. Schwille, Lynwood H. Smith, William G. Robertson, and Winfried Vahlensieck. 997 pp, illustrated. New York, Plenum Publishing Corp, 1985. $125.00 (hardcover)

It is often difficult to fully understand the numerous factors that encourage urolithiasis. The editors of this text have successfully attempted to thoroughly cover this subject. They have gathered together most of the recent and pertinent clinical data concerning stone formation and have also included important and recent applied research findings dealing with urolithiasis.

The material presented in this volume is based on the proceedings of a meeting held in Garmisch-Partenkirchen in April 1984, in which 302 physicians from five continents participated. The text was edited by four respected international authorities who have extensively contributed to our understanding of urolithiasis. This reviewer is familiar with the qualifications of Dr William G. Robertson of Leeds, England and Dr Lynwood H. Smith of the Mayo Clinic. These two authorities assisted in the selection of contributors from countries where urinary stones are a problem. They edited the manuscripts in a clear and lucid manner. As a result most are concise, with their data clearly presented.

The text covers 971 pages, including appropriate references at the end of each contribution. The index was prepared by Dr Ruemenapf of West Germany and is complete for major topics and subtopics. The subject material is divided into nine sectional headings that include the following: genetic factors related to stone disease; environmental, nutritional, gastrointestinal and metabolic factors; renal aspects of urolithiasis; the physico-chemical aspects of stone formation; the mode of actions of drugs preventing stone formation; and recent developments regarding the urological and surgical removal of stones.

The text also provides information from three round table discussions in which the participants debated the theoretical aspects of stone formation in the urinary tract, the measurement of inhibitory activity in the urine, the treatment of idiopathic stones with drugs, and the nature and subsequent treatment of calculi arising from urinary tract infection.

Perhaps a major criticism is that the papers in the text deal with important topics in a cursory fashion. Also, the tables and figures are brief in both number and content. However, appropriate references for particular subtopics are listed at the end of each paper, and this is a major asset of the work.

For any major conventional discussion of urolithiasis, a specialized textbook on urology or internal medicine would serve the purpose. Since many metabolic studies and related research studies affecting urolithiasis are not compiled in one textbook, investigators may have difficulty finding a suitable text. The organization and style as well as technical features of this book make it outstanding and unique. Most interested physicians who have had patients or family members afflicted with stone disease will find this text worth purchasing. It is also a useful reference volume.

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DECISION MAKING IN GASTROENTEROLOGY

By Joel S. Levine, MD. 378 pp, illustrated. Philadelphia, B.C. Decker, Inc., 1985. $49.50 (hardcover)

This book is one of a "clinical decision making" series covering various fields of medicine and surgery. It seems suited to almost any level of gastroenterologic sophistication. There is an extensive series of algorithms covering most gastrointestinal conditions. Each algorithm has a point of departure from which there is a logical progression of alternatives that suggest rational diagnostic or management conclusions. The starting point may be a gastroenterologic symptom or sign, a presumed diagnosis, or something as general as the need for nutritional assessment or a particular gastroenterologic procedure. Each algorithm follows a line of sequential reasoning that presumably mimics the logical approach of the clinician in his management of the patient with a gastrointestinal problem.

A valuable feature of this book is the cross-referencing of other relevant algorithms. In addition, each page containing an algorithm has a parallel page of explanatory notes to which reference is made in the algorithm. There is even a brief and highly pertinent up-to-date bibliography.

Although this is not a textbook in the classic sense, it is nevertheless highly efficient and retains essentials but leaves out the superfluous information. If, as a clinician or student, gastroenterologic aids are employed, then this book is highly recommended. It has a minimum of waste motion, and serves as a vehicle for a brief but comprehensive study, reference, or review.

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MEDICAL ONCOLOGY. BASIC PRINCIPLES AND CLINICAL MANAGEMENT OF CANCER

Edited by Paul Calabresi, MD, Philip S. Schein, MD, and Saul A. Rosenberg, MD. 1,400 pp, illustrated. New York, Macmillan Publishing Co, 1985. $110.00 (hardcover)

The significant advances in our understanding of the biology and treatment of virtually every variety of malignancy over the past 20 years has led to the establishment of medical oncology as a subspecialty of internal medicine. A consequence of the burgeoning of this new arena of clinical endeavor has been the proliferation of a number of texts that attempt to classify, organize, and coordinate a vast corpus of knowledge and experience for a heterogeneous audience involved in the care of the cancer patient. The task has proven far too vast even for the most distinguished oncologic specialists. Consequently, a large number of contributors, each writing a relatively small proportion of the text, has been the usual format employed.

This latest contender to the growing list of such comprehensive oncology textbooks, edited by three distinguished oncologists, weighs in at just under ten pounds and is written by 86 contributors "from many institutions with wide geographic distribution." The 51 chapters are organized into three major sections: Basic Principles, Specific Neoplasms, and Supportive Care. The broad scope employed results in a text valuable to many potential users including medical students, oncology fellows, nurses, surgeons, radiation oncologists, and internists. This format, however, ultimately suffers from a degree of uneveness and discontinuity common to multi-authored texts. Some of the 25 chapters covering specific neoplasms lack depth. Their uniform arrangement according to a specific organizational format results in difficult reading. Nevertheless, many of these chapters give the reader an accurate, comprehensive, and authoritative overview of the current status of a particular malignancy. The chapters covering lymphoma, breast cancer, and pediatric, gynecologic, and testicular neoplasms are exemplary. The chapters on neoplasms of the anus and esophagus fail to adequately depict the increasingly important role of combined chemoradiation regimes as a definitive treatment currently replacing the radical surgical procedures more comprehensively covered. Additionally, the authors of the anal cancer chapter misquote references on chemoradiation.

The chapters entitled "Paraneoplastic Phenomena," "Oncologic Emergencies," and "Special Complications" are particularly recommended for medical oncologists and internists. Ironically, the medical oncologist is likely to discover that much of the information needed on a daily basis is either lacking or too superficially covered in a text of this type to spare him the necessity of researching the literature. For example, the text is devoid of information pertaining to the natural history and treatment of neoplasia occurring during pregnancy; the natural history of primary peritoneal papillary carcinoma and how its management differs from that of ovarian cancer; and the treatment of colon cancer arising in association with inflammatory bowel disease. Also, in view of the increasing interest in the sequential or synchronous use of radiotherapy and chemotherapy, a chapter devoted to the pharmacokinetics of the interaction between these treatment modalities should have been included.

In a vast specialty that is rapidly evolving and changing, a textbook is often a snapshot rather than a movie of the state of the art. Consequently, texts of this type have a short half-life and a high price tag. Despite these shortcomings this text will be a useful addition to the libraries of many cancer care providers.

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ILLUSTRATED ENCYCLOPEDIA OF DERMATOLOGY

Second Edition. By Lionel Fry, MD, Fenella T. Wojnarowska, MD, and Parvin Shahrad, MD. 576 pp, illustrated. Oradell, NJ, Medical Economics Co., 1985. $29.95 (casebound)

I must admit to being prejudiced against medical encyclopedias and dictionaries. In medical school I was required to buy, at considerable expense, *Stedman's Medical Dictionary*. I have yet to open it. In general, encyclopedias cover material not in a comprehensive manner but rather superficially. Moreover, the title *Illustrated Encyclopedia of Dermatology* sounds a great deal like one of Richard Scary's series of books for children, perhaps *Illustrated Book of Cars*.

In this case, however, "encyclopedia" really seems to refer to the fact that the content of the book is organized in alphabetical order. The avowed purpose of the book is to "be helpful to those embarking on a career in dermatology and to general practitioners with a special interest in this field." Actually, I do not believe that

this book will be helpful to dermatology residents. On the contrary, residents are generally required to have extensive and detailed knowledge, far beyond the scope of this book. This book may indeed provide more help to nondermatologists with a special interest in the field. This is emphasized because in order to use this book, one must have already made a diagnosis. Thus in order to read about pemphigus, the diagnosis must have already been made. The more standard dermatology text is organized in such a way as to help in the diagnosis. If a patient has bullae, one may look up a chapter on bullous diseases and work through the characteristics until the diagnosis is made.

Having said all this, I must now admit that I loved this book, but for completely different reasons than the authors may have intended. Frequently in my practice I share published material with patients when I would like them to know more about their disease. If I diagnose pityriasis rosea, and the patient has never heard of it, I can show him that his skin condition really does fit the pattern of the disease, and I have not simply made it up. This book is absolutely perfect for that purpose. Since the disorders are in alphabetical order, I do not have to search through an index. All of the manifestations are discussed and grouped in a few pages, so that it is not necessary to look for oral manifestations in one part and ocular in another. The writing is exceptionally concise and clear. The organization is consistent. Every disease is broken down into seven parts—presentation, differential diagnosis, investigations, etiology, treatment, genetics, and prognosis, all on one or two pages. All disease entries have diagrams noting the distribution of the lesions. Other diagrams and tables deal with sex, age ratios, or drugs known to cause a certain type of eruption. Black and white photographs, for the most part, are merely adequate and in some cases not very good.

In summary, I believe that every practicing dermatologist should have this book on their shelf. It is perfect for that busy day, with a waiting room full of patients, when you have about one minute to refresh your memory of a disease. It is even more ideal as an educational tool for patients. It is bound to become one of the most used books on my shelf.

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DISEASES OF BLOOD VESSELS

By Orville Horowitz, MD, Peter R. McCombs, MD, Brooke Roberts, MD. 429 pp, illustrated. Philadelphia, Lea & Febiger, 1985. $52.00 (hardcover)

The stated theme of this book is "to suggest certain modes of treatment but simultaneously to give proper representation to divergent thoughts by supplying scientific background for the reader's consideration." The authors are primarily interested in supplying data to practicing physicians and surgeons, who must marshal their energies and thoughts on behalf of their patients. An additional theme is "an effort to supply readers with knowledge to make up their own minds concerning the controversial subjects evident in every chapter."

The book does not live up to this aim. Some sections are sparse, specifically the description of atherogenesis. The chapter on thrombogenesis is overwhelming in its complexity, while the neighboring chapter on anticoagulant therapy is quite limited in its scope and is in the nature of a set of directions for therapy.

The chapter on the approach to the patient, presumably with diseases of the blood vessels, devotes most of its attention to clinical considerations as they refer to lower extremity ischemia. The chapter on cerebrovascular disease is the only one that attempts to live up to the introductory statement with a good discussion of conflicting points of view and a reasonably thorough bibliography for such an extensive subject. There are chapters on diseases of coronary arteries, on the thoracic aorta, on the abdominal aorta and its major branches, on the urogenital circulation, on the arteries of the extremities, and, in addition, on giant cell arteritis, venous thrombosis, and indications for thrombolytic therapy, with chapters on liver circulation and lymphatic circulation. As a final effort there are chapters on noninvasive testing and angiography.

The organization of the chapters is confusing by not appearing to adhere to a particular pattern.

I am not certain as to what level of expertise the book is directed. There are chapters that are much too complex for any except those entirely devoted to a particular field, such as coagulation, while other chapters are woefully short, such as the one covering indications for thrombolytic therapy by an authority as eminent as Saul Sherry.

The total effort might have been more attractive if perhaps the chapters were better organized and better balanced.

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New type of vaccine under development may increase areas of immunity

According to JAMA (1986; 255:447–448), a new type of vaccine is being developed in experimental animals and reportedly has produced immunity against numerous viruses, bacteria, and other parasites. Unlike conventional vaccines, however, no pathogenic antigen is needed to stimulate the host's immunity. Instead, an idiotype—the site where an antigen binds to an antibody—may itself act as an antigen to stimulate antibody production. Antibodies that are stimulated by idiotypes are called anti-idiotype antibodies.

If the idiotype could be represented by a domino with four dots, the antigen might be a four-two combination, and the anti-idiotype antibody might be a four-three combination. Both will hook up with the idiotype even though they are different "molecules."

"Large scale use of this kind of (immune) network intervention, if you will, is going to be important in instances where conventional vaccines don't work, and are not necessarily to supplant conventional vaccines that are perfectly adequate," said Kathryn Stein, PhD, a research chemist in the Division of Bacterial Products, Office of Biologic Research and Review, Food and Drug Administration, Rockville, MD.

The vaccine would be particularly appealing if it could be directed against infectious organisms coated with polysaccharide capsules, to which infants cannot respond immunogenically until the age of about two years, said Joseph M. Davies, MD, PhD, professor and chairman, Department of Microbiology and Immunology, Washington University School of Medicine, St Louis.

Gordon Dreesman, PhD, chairman of the Department of Virology and Immunology, Southwest Foundation for Biomedical Research, is considering the possibility of an anti-idiotype vaccine against acquired immunodeficiency syndrome. He is among those seeking to locate the antigenic determinants of the human T-cell lymphotropic virus type three (HTLV-III) for an anti-idiotype vaccine. The research is still in its preliminary stages.

It is debatable how far in the future this technique will be tried in humans. Some researchers suggest it will be in several years, others say not at least for a decade.

Massachusetts physicians get new journal

The Massachusetts Medical Society began the publication of a new magazine, *Massachusetts Medicine*, in January of 1986. John C. Ayres, MD, editor of the new journal, said the purpose of the publication is to present a forum for news, opinion, information, and letters, allowing Massachusetts physicians to take part in the reshaping of the medical profession in Massachusetts. The Massachusetts Medical Society also publishes the *New England Journal of Medicine*.

New long-term contraceptive successful in trials

The NORPLANT system, using hormonal implants for long-term contraception, appears to be suitable for many women of reproductive age, and may eventually be available in the United States, the *Western Journal of Medicine* recently reported (1986; 144:68).

The NORPLANT system consists of six silastic capsules implanted subdermally into the upper arm, releasing into the tissue (and ultimately the bloodstream) the active ingredient, progestin levonorgestrel. This prevents conception by inhibiting ovulation, thickening cervical mucous, and suppressing endometrial activity. Field trials now cover more than 50,000 months of woman-use. Its efficacy is roughly comparable to that of tubal sterilization. In a four-year clinical study, the annual pregnancy rate was generally below 0.5 per 100 woman-years, and the cumulative five-year pregnancy rate in 992 initial acceptors was 2.7 per 100 continuous users. Fertility promptly returned following removal. Side effects, such as breakthrough bleeding, irregular menses, and occasional intermenstrual spotting or amenorrhea are considered typical of contraceptives based on continuous administration of a progestin.

The six-capsule formulation has been approved for distribution in Finland, and is under consideration by the Food and Drug Administration for approval in the United States. The six-capsule NORPLANT is likely to receive approval more quickly than a newer two-capsule version because of its lengthier period of study. The two-capsule version is currently undergoing field trials.

Seatbelt use permanently mandated in Great Britain

Great Britain remains ahead of the United States in efforts to mandate the use of seatbelts by drivers and front seat passengers of cars and vans, with its January 13th decision to continue the 1981 law requiring the use of seatbelts. According to the *Lancet* (1986: i;224), only 25 members of Parliament voted against the measure to make the law permanent. (217 members of Parliament voted in favor of the measure.) The overwhelmingly affirmative vote came in spite of the fact that the statistics of lives saved and accidents prevented have not lived up to the Department of Transport's original expectations: between 207 and 459 deaths are now calculated to be saved each year by seatbelt use (instead of the 1,000 originally predicted) and 7,600 serious injuries prevented (instead of 10,000). The *Lancet* predicted that disappointment would exist because the statistics indicated the measure has fallen short of its promise (1986: i;75–76) and anti-belt advocates did mention the discrepancy in the figures. However, convincing evidence does exist in trends observed in 14 of 15 hospital accident departments that took part in a study of casualties brought in during the year before and after the seatbelt law went into effect. Patients taken to hospi-

tals fell in number by 15%, and the number needing admission to the hospital fell by one quarter, as reported in the *Lancet*.

1985 Association of American Publishers Awards announced

Under the auspices of the Professional and Scholarly Publishing (PSP) division of the Association of American Publishers, a panel of independent judges from the publishing industry, and the industrial, medical, and scientific communities convened to judge more than 235 professional and scholarly works in competition for the 10th Annual Professional and Scholarly Books Awards. The following awards were announced:

Best Creative and Innovative New PSP Project: Human skeleton 35-inch functional scale model, designed by Leon Schlossberg, published by the Johns Hopkins University Press.

Best Health Sciences Books: *Diagnostic Imaging in Internal Medicine*, by Ronald L. Eisenberg, MD, and published by McGraw-Hill Book Company. Honorable Mention: *Clinical Dermatology: A Color Guide to Diagnosis and Therapy*, by Thomas P. Habif, MD, and published by C.V. Mosby Company.

Best New Journal in Science/Technology/Medicine: *Emergency Care Quarterly*, edited by Lenworth M. Jacobs, Jr, MD, and Barbara R. Bennett, RN, and published by Aspen Publishers, Inc. Honorable Mention: *Journal of Electron Microscopy Technique*, edited by John E. Johnson, Jr, and published by Alan R. Liss, Inc.

Best Social and Behavioral Sciences Books: *A Century of Psychology As Science*, edited by Sigmund Koch and David D. Leary, and published by McGraw-Hill Book Company. Honorable Mention: *The Divorce Revolution: The Unexpected Social and Economic Consequences for Women and Children in America*, by Lenore J. Weitzman, and published by The Free Press, Professional Books Division, Macmillan Publishing Company; and *Religion in American Public Life*, by A. James Reichley, and published by The Brookings Institution.

Best Single Issue of a Journal: Topics in Geriatric Rehabilitation, Volume 1, Number 1: *Exercise and Aging*, edited by Carole Bernstein Lewis, PT, PHD, and Everett L. Smith, PHD, and published by Aspen Publishers, Inc. Honorable Mention: *Medical Heritage*, Volume 1, Number 5, edited by Sharon Romm, MD, and published by W.B. Saunders Company.

NEWS BRIEFS are compiled and written by Sandra Cirincione.

25th anniversary of Health Research Training Program

With a proclamation from Mayor Edward I. Koch, public health officials and others celebrated the 25th anniversary of the Health Research Training Program on February 5th.

"This program . . . has fostered and facilitated significant public health investigation; it serves to benefit the student participants, the preceptors who guide its activities, and the City of New York that gains a potential pool of talented public health professionals," Mr Koch said, in proclaiming February 5th to be Health Research Training Program Day.

The Health Research Training Program provides college students with the opportunity to participate in public health research and administration projects. Under the guidance of physicians and administrators, approximately 200 students work on projects in the five boroughs of New York City at health department sites and other non-profit institutions.

The work of students from the Health Research Training Program has had significant impact on public health in New York City. Operational changes in program delivery and in the New York City health code have resulted from Health Research Training Program work. Numerous graduates of the program have returned to assume positions in the Department of Health; one graduate went on to become the city's Commissioner of Health.

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

J. Edward Astrachan, MD, Queens Village. Died October 20, 1985; age 78. He was a 1930 graduate of the University of Michigan Medical School. Dr Astrachan was a Qualified Fellow of the International College of Surgeons and a member of the American Society of Colon and Rectal Surgeons, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Peter Anton Badamy, MD, Rochester. Died October 6, 1985; age 77. Dr Badamy was a 1934 graduate of Georgetown University School of Medicine, Washington. He was a Qualified Fellow of the International College of Surgeons and a member of the Academy of Medicine, the American Geriatrics Society, the Pan American Association of Ophthalmology, the Medical Society of the County of Monroe and the Medical Society of the State of New York.

Howard Taft Behrman, MD, New York. Died October 9, 1985; age 73. He was a 1938 graduate of New York University College of Medicine. Dr Behrman was a Diplomate of the American Board of Dermatology, Inc. and a member of the Academy of Medicine, the New York State Dermatological Society, the American Academy of Dermatology, the American Academy of Compensation Medicine, Inc., the Society for Investigative Dermatology, the New York County Medical Society and the Medical Society of the State of New York.

Howard E. Berk, MD, Forest Hills. Died October 22, 1985; age 81. He was a 1945 graduate of the Chicago Medical School. Dr Berk was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychiatric Association, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Walter William Brandes, MD, Hampton Bays. Died September 18, 1985; age 86. He was a 1937 graduate of Northwestern University Medical School, Chicago. Dr Brandes was a Fellow of the American College of Pathologists, a Diplomate of the American Board of Pathology, and a member of the Academy of Medicine, the American Association of Pathologists and Bacteriologists, the American Society for Experimental Pathology, the New York County Medical Society and the Medical Society of the State of New York.

James Francis Butler, MD, Boynton Beach, Florida. Died December 3, 1985; age 76. He was a 1936 graduate of Georgetown University School of Medicine, Washington. Dr Butler was a member of the American Academy of Family Practice, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Julius Chasnoff, MD, New York. Died December 3, 1985; age 83. He was a 1926 graduate of Cornell University Medical College. Dr Chasnoff was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. He was a member of the Academy of Medicine, the New York County Medical Society and the Medical Society of the State of New York.

George Frederick Christ, MD, Port Jefferson. Died October 28, 1985; age 50. Dr Christ was a 1961 graduate of Creighton University School of Medicine, Omaha. He was a member of the American Academy of Family Practice, the Suffolk County Medical Society and the Medical Society of the State of New York.

George Jarvis Coffin, MD, New York. Died October 2, 1985; age 90. Dr Coffin was a 1921 graduate of New York University College of Medicine. His memberships included the New York County Medical Society and the Medical Society of the State of New York.

David Harvey Cohen, MD, Flushing. Died October 15, 1985; age 74. Dr Cohen was a 1939 graduate of New York University College of Medicine. His memberships included the American Thoracic Society, the Medical Society of the County of Queens and the Medical Society of the State of New York.

David Dominic Colucci, MD, Webster. Died September 16, 1985; age 76. Dr Colucci was a 1939 graduate of Creighton University School of Medicine, Omaha. He was a member of the Academy of Medicine, the Medical Society of the County of Monroe and the Medical Society of the State of New York.

Michael Joseph Cronmiller, MD, Rochester. Died October 3, 1985; age 82. Dr Cronmiller was a 1940 graduate of St. Louis University School of Medicine. He was a Fellow of the American Academy of Family Physicians, and a member of the Academy of Medicine, the Medical Society of the County of Monroe and the Medical Society of the State of New York.

George Alexander Friedman, MD, New York. Died December 14, 1985; age 75. Dr Friedman was a 1936 graduate of Eotvos Lorand Tudomanyegyetem Orvostudomanyi Fakultas, Budapest. He was a member of the New York State Surgical Society, the New York County Medical Society and the Medical Society of the State of New York.

William E. Gannon, MD, Malverne. Died October 3, 1985; age 62. He was a 1952 graduate of the State University of New York Downstate Medical Center. Dr Gannon was a Fellow of the American College of Radiology, a Diplomate of the American Board of Radi-

ology, the Radiological Society of North America, Inc., the American Roentgen Ray Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Steven S. Gorman, MD, Rego Park. Died December 12, 1985; age 42. He was a 1981 graduate of St. Georges University School of Medicine. Dr Gorman was a Fellow of the American College of Physicians, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Merrill Patterson Haas, MD, Suffern. Died December 2, 1985; age 73. Dr Haas was a 1938 graduate of Columbia University College of Physicians and Surgeons. He was a member of the Academy of Medicine, the American Academy of Pediatrics, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Jarmila Helen Hasek, MD, Pomona. Died November 26, 1985; age 47. She was a 1962 graduate of Masarykova Università Fakultà Lekarska, Brno. Dr Hasek was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, a Diplomate of the American Board of Obstetrics and Gynecology, and a member of the Medical Society of the County of Rockland and the Medical Society of the State of New York.

Nathaniel Robert Hermann, MD, New York. Died December 12, 1985; age 81. He was a 1930 graduate of New York University College of Medicine. Dr Hermann was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Urology, and a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

William C. Hollis, MD, Mineola. Died October 14, 1985; age 59. He was a 1950 graduate of Cornell University Medical College. Dr Hollis was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the Clinical Society of the New York Diabetes Association, the New York State Society of Internal Medicine, the Endocrine Society, the American Society of Internal Medicine, the Nassau County Medical Society and the Medical Society of the State of New York.

Martin Jacobs, MD, Chevy Chase, Maryland. Died October 6, 1985; age 77. Dr Jacobs was a 1932 graduate of the State University of New York Downstate Medical Center. He was a member of the American Geriatrics Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Edward A. Kearney, MD, Cornwall. Died December 5, 1985; age 75. He was a 1936 graduate of Columbia University College of Physicians and Surgeons. Dr Kearney was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Surgery. His memberships included the Academy of Medicine, the Medical Society of the County of Orange and the Medical Society of the State of New York.

Paul Emanuel Klein, MD, New York. Died June 6, 1985; age 89. Dr Klein was a 1923 graduate of Medizinische Fakultät der Universität, Wien. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Leila C. Knox, MD, Parish. Died October 13, 1985; age 102. Dr Knox was a 1918 graduate of Cornell University Medical College. She was a member of the New York County Medical Society and the Medical Society of the State of New York.

John Kraai, MD, Fairport. Died September 14, 1985; age 76. Dr Kraai was a 1933 graduate of the University of Rochester School of Medicine and Dentistry. He was a member of the Medical Society of the County of Monroe and the Medical Society of the State of New York.

David Leonard Lerner, MD, Plantation, Florida. Died September 4, 1985; age 80. Dr Lerner was a 1934 graduate of the University of Illinois College of Medicine. He was a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Anthony E. Loscalzo, MD, Mt. Kisco. Died October 4, 1985; age 79. He was a 1932 graduate of the State University of New York Downstate Medical Center. Dr Loscalzo was a member of the Academy of Medicine, the American Psychiatric Association, the American Academy of Neurology, the American Geriatrics Society, the Association for Research in Nervous and Mental Disease, the New York County Medical Society and the Medical Society of the State of New York.

Henry J. Lowenfeld, MD, New York. Died September 23, 1985; age 85. He was a 1925 graduate of Universität Heidelberg Medizinische Fakultät, Baden. Dr Lowenfeld was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychoanalytic Association, the American Psychiatric Association, the New York County Medical Society and the Medical Society of the State of New York.

Margaret S. Mahler, MD, New York. Died October 2, 1985; age 88. She was a 1923 graduate of Thuringische, Landesuniversität Medizinische Fakultät, Jena, Thuringia. Dr Mahler was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychoanalytic Association, the American Psychiatric Association, the American Academy of Child Psychiatry, the New York County Medical Society and the Medical Society of the State of New York.

Malcolm Judd Mann, MD, Ithaca. Died September 27, 1985; age 71. He was a 1939 graduate of Cornell University Medical College. Dr Mann was a Fellow of the American College of Physicians, a Diplomate of the American Board of Internal Medicine, and a member of the Medical Society of the County of Tompkins and the Medical Society of the State of New York.

John Sanders Miller, Jr., MD, Bridgeport, Connecticut. Died October 7, 1985; age 78. Dr Miller was a 1934 graduate of Johns Hopkins University School of Medicine, Baltimore. He was a member of the Medical Society of the County of Essex and the Medical Society of the State of New York.

William Asa Milner, MD, Albany. Died October 3, 1985; age 81. Dr Milner was a 1930 graduate of the State University of Iowa College of Medicine, Iowa City. He was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Urology. Dr Milner was a member of the American Urological Association, the American

Academy of Pediatrics, the Medical Society of the County of Albany and the Medical Society of the State of New York.

Arthur Minsky, MD, Jamaica. Died October 7, 1985; age 76. He was a 1934 graduate of George Washington University School of Medicine. Dr Minsky was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Ophthalmology, and a member of the New York Society for Clinical Ophthalmology, the American Academy of Ophthalmology and Otolaryngology, the Pan American Association of Ophthalmology, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Anthony Joseph Morreale, MD, Middletown. Died September 20, 1985; age 79. Dr Morreale was a 1932 graduate of the University of Rochester School of Medicine and Dentistry. He was a Fellow of the American College of Surgeons and a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

Theodore Neustaedter, MD, Little Neck. Died December 21, 1985; age 86. He was a 1924 graduate of the University of Maryland School of Medicine, Baltimore. Dr Neustaedter was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the New York County Medical Society and the Medical Society of the State of New York.

Laurence Charles Older, MD, Cuba. Died November 28, 1985; age 81. Dr Older was a 1929 graduate of New York University College of Medicine. He was a member of the Medical Society of the County of Allegany and the Medical Society of the State of New York.

Andrew Peto, MD, New York. Died April 22, 1985; age 81. He was a 1929 graduate of Eotvos Lorand Tudomanyegyetem Orvostudomanyi Fakultas, Budapest. Dr Peto was a member of the American Psychoanalytic Association, the American Psychiatric Association, the New York County Medical Society and the Medical Society of the State of New York.

Nathan Portnoy, MD, New York. Died October 9, 1985; age 90. Dr Portnoy was a 1918 graduate of New York University College of Medicine. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Lewis Bernard Posner, MD, Bronx. Died December 22, 1985; age 83. Dr Posner was a 1929 graduate of New York University College of Medicine. He was a Fellow of the American College of Obstetricians and Gynecologists and a Qualified Fellow of the International College of Surgeons. Dr Posner was a member of the New York County Medical Society and the Medical Society of the State of New York.

Maurice Rashbaum, MD, New York. Died December 11, 1985; age 92. Dr Rashbaum was a 1917 graduate of New York University College of Medicine. He was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Academy of Medicine, the New York County Medical Society and the Medical Society of the State of New York.

Jane L. Ross, MD, New York. Died October 7, 1985; age 36. She was a 1974 graduate of New York University College of Medicine. Dr Ross was a Diplomate of the American Board of Internal Medicine and a member of the American Medical Women's Association, the New York County Medical Society, and the Medical Society of the State of New York.

Louis J. Scordamaglia, MD, East Patchogue. Died December 14, 1985; age 60. He was a 1949 graduate of Marquette University School of Medicine, Milwaukee. Dr Scordamaglia was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Urology, and a member of the American Urological Association, the Suffolk County Medical Society and the Medical Society of the State of New York.

Menahem Shaham, MD, Emeryville, California. Died August 14, 1985; age 79. He was a 1934 graduate of the Università Karlova Fakultà Lekarska, Praha. Dr Shaham was a member of the New York Society of Physical Medicine and Rehabilitation, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Lucy Shimmerlik, MD, Port Washington. Died November 21, 1985; age 88. She was a 1923 graduate of Deutsche Universität Medizinische Fakultät, Prague. Dr Shimmerlik was a member of the American Fertility Society, the Medical Society of the County of Queens and the Medical Society of the State of New York.

Reuben B. Silverstein, MD, Beechhurst. Died November 25, 1985; age 80. He was a 1929 graduate of New York Medical College, Flower and Fifth Avenue Hospital. Dr Silverstein was a Fellow of the American College of Angiology and the American Academy of Family Physicians. His memberships included the New York Cardiological Society, the American Geriatrics Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Warren Milford Tarter, MD, Beacon. Died September 5, 1985; age 54. Dr Tarter was a 1961 graduate of Université Libre de Bruxelles Faculté de Medecine. He was a member of the Dutchess County Medical Society and the Medical Society of the State of New York.

Clayton Homer Thomas, MD, Medina. Died November 12, 1985; age 89. Dr Thomas was a 1923 graduate of the University of Toronto Faculty of Medicine. He was a member of the Medical Society of the County of Orleans and the Medical Society of the State of New York.

George A. Wagner, MD, Lehigh Acres, Florida. Died August 14, 1985; age 89. Dr Wagner was a 1920 graduate of New York University College of Medicine. He was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

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Sick Neonates. Info: Arthur J. Schwager, MD, Director, Continuing Pediatric Medical Education, Huntington Hospital, Park Ave, Huntington, NY 11743. Tel: (516) 427-0530.

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Apr 1. **AIDS: State of the Art and Prospects for the Future.** Tarrytown Hilton. Info: Pathology Department, New York Medical College, Valhalla, NY 10595. Tel: (914) 993-4487.

Apr 22. **Immunological Approaches to Colon Cancer.** 1 Cat 1 Credit. **Management of Recurrent Colorectal Cancer.** 1 Cat 1 Credit. Info: Westchester Medical Society, 84 Purchase St, Purchase, NY 10577. Tel: (914) 948-4100.

ROCKLAND

Apr 1. **Current Concepts in the Treatment and Diagnosis of Lymphoma.** 1 Cat 1 Credit. *Apr 8.* **Palliative Care of the Oncologic Patient.** 1 Cat 1 Credit. *Apr 15* **Current Concepts in the Use of Blood and Blood Products.** 1 Cat 1 Credit. *Apr 22.* **Idiopathic Thrombocytopenia.** Info: Myrna Hahn, Secretary, Department of Internal Medicine, Nyack Hospital, North Midland Ave, Nyack, NY 10960. Tel: (914) 358-6200, ext. 2509.

AROUND THE NATION

ALABAMA

Apr 4–5. **Circuit Courses in Internal Medicine.** Info: Arnold Aberman, MD, American College of Physicians, 4200 Pine St, Philadelphia, PA 19104.

CALIFORNIA

Apr 5–6. **Transurethral Ureteroscopy: A Seminar and Workshop.** 13 ½ Cat 1 Credits. Info: Continuing Medical Education, M-017, University of California San Diego School of Medicine, La Jolla, CA 92093. Tel: (619) 452-3940.

Apr 17–19. **Extended Programs in Medical Education.** 15 Cat 1 Credits. Info: Registration Office, Room 575-U, University of California, San Francisco, CA 94143-0764. Tel: (415) 476-5808.

KENTUCKY

Apr 18–19. **Contemporary Pediatrics for the Practicing Physicians.** 10 Cat 1 Credits. Info: University of Kentucky School of Medicine, Office of Continuing Education, 132 COM Office Building, Lexington, KY 40563-0086. Tel: (606) 233-5161.

MARYLAND

Apr 28–May 9. **27th Postgraduate Institute for Pathologists.** Info: John K. Frost, MD, Professor of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD 21205. Tel: (301) 955-3522.

MISSOURI

Apr 3–6. **Third International Symposium on Oral and Maxillofacial Surgery.** Info: Office of Continuing Medical Education, University of Missouri-Kansas City, 2220 Holmes, Kansas City, MO 64108. Tel: (816) 276-1339.

SOUTH CAROLINA

Apr 14–18. **Current Clinical Pediatrics.** 16 Cat 1 Credits. Hilton Head. Info: Department of Continuing Medical Education, Boston University School of Medicine, 80 East Concord St, Boston, MA 02118. Tel: (617) 638-4605.

TENNESSEE

Apr 17–18. **Oak Ridge Conference on Advanced Analytical Concepts in Chemometrics.** Knoxville. Info: AACC Meetings Department, 1725 K. St, NW, Suite 1010, Washington, DC 20006. Tel: (800) 892-1400.

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The following clearly defines what each is. After reviewing these various types of pre-paid health care, we believe you will have the basic information necessary to choose the best for you.

HEALTH MAINTENANCE ORGANIZATIONS (HMOs)

CENTER OR CLINIC

- Central facility or facilities
- Staff physicians
- Patient selects a primary care physician (Internist, GP, FP, and Pediatrician) from the staff
- May frequently have physician turnover resulting in short term doctor-patient relationship and/or the need to re-select primary physician

DIRECT PHYSICIAN CONTRACTING

- No central facility
- Private practicing physicians
- Patient selects a primary care physician (Internist, GP, FP, Pediatrician)
- Obstetrician-Gynecologist is not a primary, but a specialist. The patient is seen by the Obstetrician-Gynecologist only by referral from the primary care physician.
- Primary physicians are capitated. That means they are paid a fixed amount annually to treat a specific patient whether they see that patient once—or a hundred times.
- No group voice because there is no physician group
- Specialists are reimbursed a percentage of their fee
- Patients can see physicians when they want

IPA CORPORATIONS

- No central facility
- Private practicing physicians
- Patient selects 1 or 2 primary physicians: Female and male adults select an Internist, GP or FP; females additionally select an Obstetrician-Gynecologist; parents select a Pediatrician, GP or FP for their child(ren).

  Obstetrician-gynecologists are primary care physicians, and can be seen directly by the member for both routine and specialized care with no referral necessary.
- A corporate body which is organized by physicians. The IPA then contracts with an HMO to provide services to the HMO members. *The physician does not join the HMO, but simply participates.*
- The IPA is the physicians' voice to the HMO which represents the physician re: fee reimbursement, quality of care, peer review, etc.
- Traditional fee-for-service payment
- Patients can see physicians when needed. Each visit is paid for by the HMO on a fee-for-service basis

EXAMPLES

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If you have further questions regarding any of the above, call HealthWays' IPA Department at 1-800-624-0720 in New Jersey or 201-636-6200 out-of-state.

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AIDS

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AIDS is just the tip of the HTLV-III infection iceberg. Sources estimate the number of individuals in the United States infected with HTLV-III at one to two million.[1,2] Thus, one of your patients may soon present with some form of HTLV-III disease.

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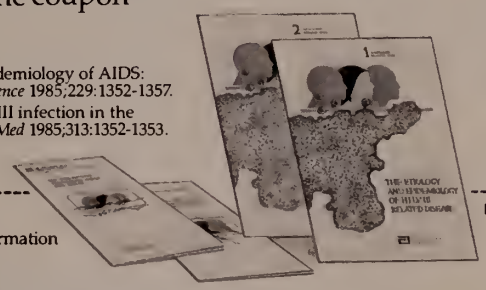
References: 1. Curran JW *et al*: The epidemiology of AIDS: Current status and future prospects. *Science* 1985;229:1352-1357.
2. Sivak SL *et al*: How common is HTLV-III infection in the United States? Correspondence. *N Engl J Med* 1985;313:1352-1353.



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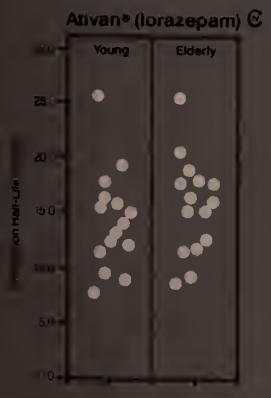

Ativan®, which is *conjugated* rather than oxidized, shows little difference in half-life ($t\frac{1}{2}$) between young and elderly subjects[2]

References

1. Greenblatt DJ: Clinical study, pharmacokinetics and bioavailability in the elderly, Ativan® (lorazepam). Data on file, Wyeth Laboratories.
2. Greenblatt DJ, Allen MD, Locniskar A, et al: Lorazepam kinetics in the elderly. Clin Pharmacol Ther 26:103-113, 1979.

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Brief Summary of Prescribing Information.

Indications and Usage: Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic.

Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

Contraindications: Known sensitivity to benzodiazepines or acute narrow-angle glaucoma

Warnings: Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

Physical and Psychological Dependence: Withdrawal symptoms like those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, e.g. drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months.

Precautions: In depression accompanying anxiety, consider possibility for suicide.

For elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Terminate dosage gradually since abrupt withdrawal of any antianxiety agent may result in symptoms like those being treated: anxiety, agitation, irritability, tension, insomnia and occasional convulsions. Observe usual precautions with impaired renal or hepatic function. Where gastrointestinal or cardiovascular disorders coexist with anxiety, note that lorazepam has not been shown of significant benefit in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 6 times maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment was withdrawn within 2 months of first observation. Clinical significance is unknown; but use of lorazepam for prolonged periods and in geriatrics requires caution and frequent monitoring for symptoms of upper G.I. disease. Safety and effectiveness in children under 12 years have not been established.

ESSENTIAL LABORATORY TESTS: Some patients have developed leukopenia; some have had elevations of LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

CARCINOGENESIS AND MUTAGENESIS: No evidence of carcinogenic potential emerged in rats during an 18-month study. No studies regarding mutagenesis have been performed.

PREGNANCY: Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although all these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of discontinuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

NURSING MOTHERS: It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

Adverse Reactions, if they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%) and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbance, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and unsteadiness increased with age. Small decreases in blood pressure have been noted but are not clinically significant, probably being related to relief of anxiety.

Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

Overdosage: In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce vomiting and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol Bitartrate Injection U.S.P. Usefulness of dialysis has not been determined.

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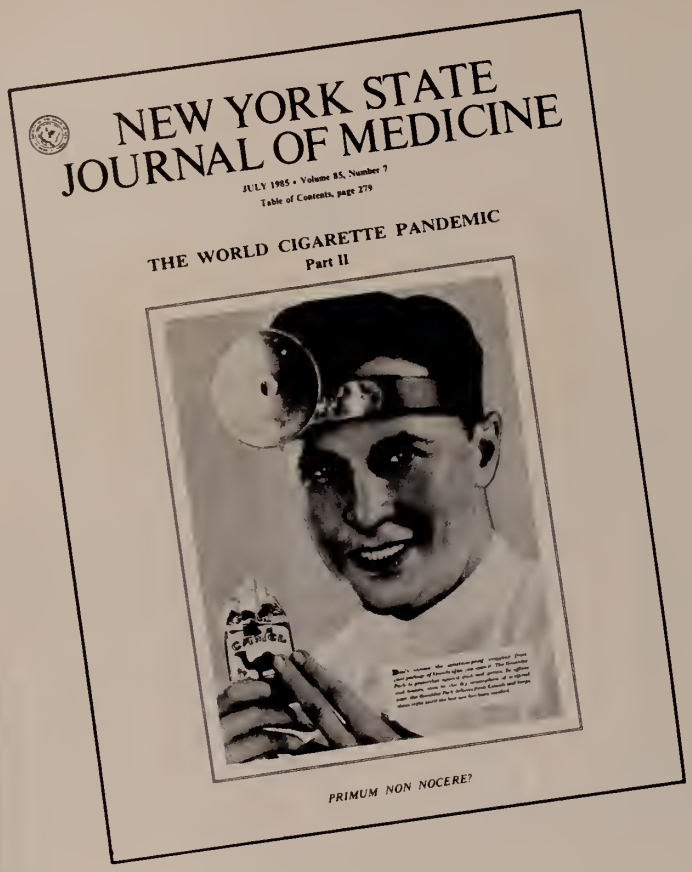

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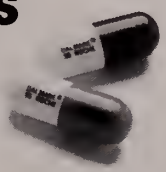

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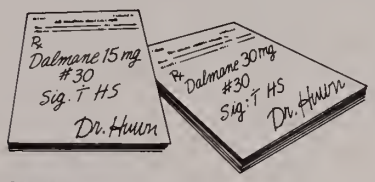

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Indications: Effective in oll types of insomnia chorocterized by difficulty in falling asleep, frequent nocturnol owokenings and/or eorly morning owokening; in potients with recurring insomnio or poor sleeping hobits; in ocute or chronic medicol situotions requiring restful sleep. Objective sleep loborotory doto hove shown effectiveness for ot leost 28 consecutive nights of odministration. Since insomnio is offen transient ond intermittent, prolonged odministrotion is generolly not necessory or recommended. Repeoted theropy should only be undertoken with oppropriote potient evoluation.

Contraindcatians: Known hypersensitivity to flurozepom HCl; pregnoncy. Benzodiozepines moy couse fetol domoge when odministered during pregnoncy. Severol studies suggest on increosed risk of congenitol molformotions ossocioted with benzodiazepine use during the first trimester. Warn patients of the potentiol risks to the fetus should the possibility of becoming pregnont exist while receiving flurozepom. Instruct patients to discontinue drug prior to becoming pregnont. Consider the possibility of pregnancy prior to instituting therapy

Warnings: Coution potients obout possible combined effects with alcohol ond other CNS depressonts. An additive effect moy occur if alcohol is consumed the doy following use for nighttime sedotion. This potentiol moy exist for severol doys following discontinuotion. Caution against hazardous occupotions requiring complete mental alertness (*e g*, operoting mochinery, driving). Potentiol impairment of performonce of such octivities moy occur the doy following ingestion. Not recommended for use in persons under 15 yeors of oge. Withdrowol symptoms rorely reported, obrupt discontinuotion should be ovoided with groduol topering of dosage for those potients on medicotion for o prolonged period of time. Use coution in odministering to oddiction-prone individuols or those who might increose dosoge.

Precautions: In elderly ond debilitated patients, it is recommended thot the dosoge be limited to 15 mg to reduce risk of oversedotion, dizziness, confusion ond/or otoxio. Consider potentiol additive effects with other hypnotics or CNS depressonts. Employ usuol precautions in severely depressed potients, or in those with latent depression or suicidol tendencies, or in those with impoired renol or hepotic function

Adverse Reactions: Dizziness, drowsiness, lightheodedness, staggering, otoxio ond falling hove occurred, porticulorly in elderly or debilitoted potients. Severe sedotion, lethargy, disorientotion ond coma, probably indicative of drug intolerance or overdosoge, hove been reported. Also reported: heodoche, heartburn, upset stomoch, nouseo, vomiting, diorrhea, constipotion, GI poin, nervousness, folkotiveness, apprehension, irritobility, weokness, polpitations, chest poins, body ond joint poins ond GU complaints. There hove also been rore occurrences of leukopenia, granulacytopenio, sweoting, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter toste, excessive salivotion, onorexia, euphoria, depression, slurred speech, confusion, restlessness, hollucinotions, ond elevoted SGOT, SGPT, totol ond direct bilirubins, ond olkoline phosphotose, and paradoxicol reactions, *e g*, excitement, stimulotion ond hyperoctivity

Dosage: Individualize for maximum beneficiol effect. *Adults* 30 mg usuol dosoge; 15 mg moy suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initiolly until response is determined

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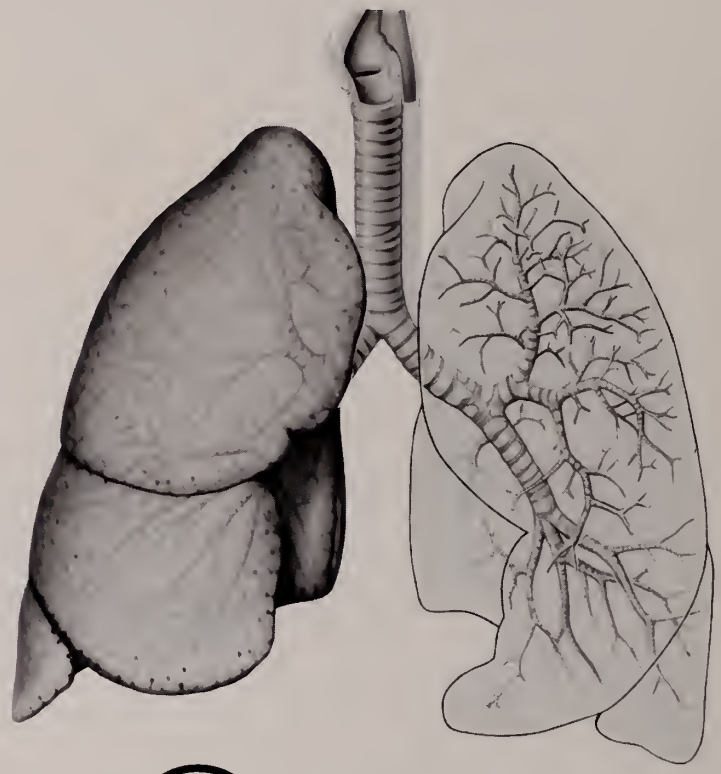

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cefaclor

250-mg Pulvules® t.i.d.

offers effectiveness against the major causes of bacterial bronchitis

H. influenzae, H. influenzae, S. pneumoniae, S. pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Brief Summary. Consult the package literature for prescribing information

Indications and Usage: Ceclor* (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Lower respiratory infections, including pneumonia caused by *Streptococcus pneumoniae (Diplococcus pneumoniae), Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci)

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

Contraindication: Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS, INCLUDING ANAPHYLAXIS, TO BOTH DRUG CLASSES.

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should be ruled out.

Precautions: *General Precautions* — If an allergic reaction to Ceclor* (cefaclor, Lilly) occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of Ceclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

As a result of administration of Ceclor, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest* tablets but not with Tes-Tape* (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy — Pregnancy Category B — Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given three times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceclor* (cefaclor, Lilly). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers — Small amounts of Ceclor have been detected in mother's milk following administration of single 500-mg doses. Average levels were 0.18, 0.20, 0.21, and 0.16 mcg/ml at two, three, four, and five hours respectively. Trace amounts were detected at one hour. The effect on nursing infants is not known. Caution should be exercised when Ceclor is administered to a nursing woman.

Usage in Children — Safety and effectiveness of this product for use in infants less than one month of age have not been established.

Adverse Reactions: Adverse effects considered related to therapy with Ceclor are uncommon and are listed below.

Gastrointestinal symptoms occur in about 2.5 percent of patients and include diarrhea (1 in 70).

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Hypersensitivity reactions have been reported in about 1.5 percent of patients and include morbiliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions (erythema multiforme or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever) have been reported. These reactions are apparently due to hypersensitivity and have usually occurred during or following a second course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.

Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.

Other effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

Causal Relationship Uncertain — Transitory abnormalities in clinical laboratory test results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

Hepatic — Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

Hematopoietic — Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

Renal — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[061782R]

Note: Ceclor* (cefaclor, Lilly) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

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In addition to effective relief of anxiety associated with depressive symptoms...

Only Ativan® (lorazepam) CIV

among leading benzodiazepines, has proof that its pharmacokinetics are not significantly altered by age.[1]

With Ativan, elimination half-life was very similar between young and elderly groups tested; differences did not approach statistical significance.[1]

Comparison of elimination half-lives in young and elderly subjects.

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Brief Summary of Prescribing Information.

Indications and Usage: Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic.

Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

Contraindications: Known sensitivity to benzodiazepines or acute narrow-angle glaucoma.

Warnings: Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

Physical and Psychological Dependence: Withdrawal symptoms like those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, e.g. drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months.

Precautions: In depression accompanying anxiety, consider possibility for suicide.

For elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Terminate dosage gradually since abrupt withdrawal of any antianxiety agent may result in symptoms like those being treated: anxiety, agitation, irritability, tension, insomnia and occasional convulsions. Observe usual precautions with impaired renal or hepatic function. Where gastrointestinal or cardiovascular disorders coexist with anxiety, note that lorazepam has not been shown of significant benefit in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 6 times maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment was withdrawn within 2 months of first observation. Clinical significance is unknown; but use of lorazepam for prolonged periods and in geriatrics requires caution and frequent monitoring for symptoms of upper G.I. disease. Safety and effectiveness in children under 12 years have not been established.

ESSENTIAL LABORATORY TESTS: Some patients have developed leukopenia; some have had elevations of LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

CARCINOGENESIS AND MUTAGENESIS: No evidence of carcinogenic potential emerged in rats during an 18-month study. No studies regarding mutagenesis have been performed.

PREGNANCY: Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although all these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of discontinuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

NURSING MOTHERS: It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

Adverse Reactions, if they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%) and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbance, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and unsteadiness increased with age. Small decreases in blood pressure have been noted but are not clinically significant, probably being related to relief of anxiety.

Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

Overdosage: In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce vomiting and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol Bitartrate Injection U.S.P. Usefulness of dialysis has not been determined.

Ativan® IV for (lorazepam) Anxiety

DOSAGE: Individualize for maximum beneficial effects. Increase dose gradually when needed, giving higher evening dose before increasing daytime doses. Anxiety, usually 2-3mg/day given b.i.d. or t.i.d.; dosage may vary from 1 to 10mg/day in divided doses. For elderly or debilitated, initially 1-2mg/day; insomnia due to anxiety or transient situational stress, 2-4mg h.s.

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May 1–3. **Plastic Surgery Update: The Face.** 24 Cat 1 Credits. Grand Hyatt Hotel. *May 12–15.* **Diagnosis and Treatment of Diseases of the Spine.** 23 Cat 1 Credits. Grand Hyatt Hotel. *May 21.* **The Eye As a Mirror of Neurological Dysfunction.** New York Neuropsychology Group. Info: NYU Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

May 7. **Current Controversial Problems in Endocrinology.** *May 9.* **Management of Stroke, Medical, Neurological, and Rehabilitation Aspects.** Info: Beverley R. Baptiste, Medical Education, Beth Israel Medical Center, First Ave at 16th St, New York, NY 10003. Tel: (212) 420-2849.

May 8–10. **Surgical Courses in Lens Implantation.** Info: Ruth Green, Administrator, Ophthalmological Foundation of America, 823 United Nations Pl, New York, NY 10017. Tel: (212) 986-4848.

May 9. **Technology and Aging in America.** Info: Johanna Cooper, Conference Coordinator, Brookdale Institute on Aging and Adult Human Development, Columbia University, 622 West 113th St, New York, NY 10025. Tel: (212) 280-2513.

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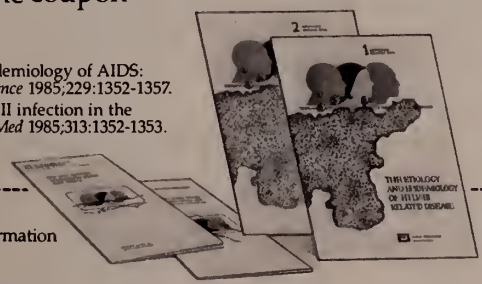

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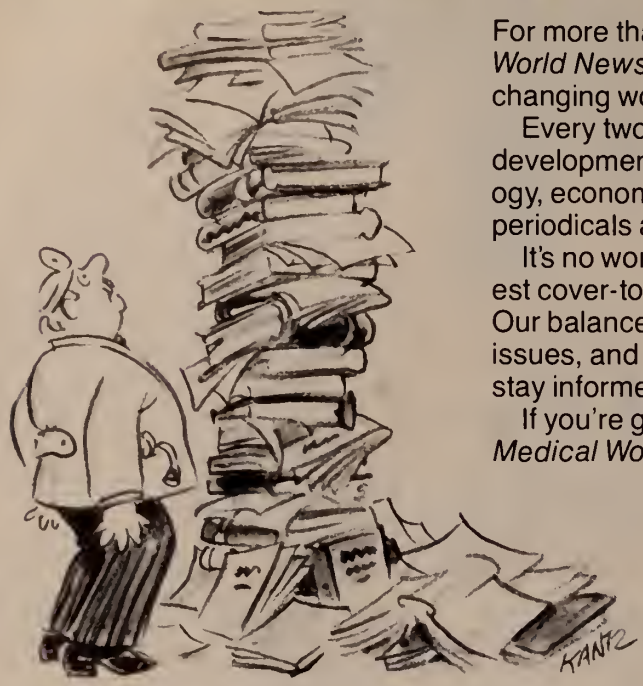

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May 15–16. **59th Annual New York Eye and Ear Infirmary Clinical Conference.** Vista International Hotel. Info: Jane Stark, Conference Registrar, New York Eye and Ear Infirmary, 310 East 14th St, New York, NY 10003. Tel: (212) 598-1430.

May 16. **Society for Urology and Engineering Annual Meeting.** New York Hilton. Info: George R. Nagamatsu, MD, Society of Urology and Engineering, 121 East 60th St, New York, NY 10022. Tel: (212) 838-5917.

May 30–31. **Rhinology Update.** 13 Cat 1 Credits. Info: Kristen M. Johnson, Administrator, Department of Otolaryngology, Manhattan Eye, Ear and Throat Hospital, 210 East 64th St, New York, NY 10021. Tel: (212) 838-9200, ext. 2448.

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May 7. **Blood Component Therapy.** Info: Division of Hematology/Oncology, Department of Medicine, Interfaith Medical Center, 555 Prospect Pl, Brooklyn, NY 12238. Tel: (718) 240-1211.

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May 1. **Second Annual Course in Practical Upper Extremity Prosthetics.** Info: Lawrence Friedmann, MD, Physical Medicine and Rehabilitation, Nassau County Medical Center, East Meadow, NY 11543. Tel: (516) 542-2525.

May 2. **The Michael M. Axinn Annual Memorial Conference on Mood Disorders and Their Effect on Creativity.** 5 Cat 1 Credits. Info: Louise Mandel, MA, Director, Department of Health Education and Community Affairs, North Shore University Hospital, 300 Community Dr, Manhasset, NY 11030. Tel: (516) 562-3045.

May 7. **GI Bleeding: Interventional Endoscopy.** *May 21.* **Controversies in Postmenopausal Hormone Therapy.** Info: Medical Education Department, Mercy Hospital, 1000 North Village Ave, Rockville Centre, NY 11570. Tel: (516) 255-2260.

May 13. **Role of Diuretics and Drug Interactions.** 1 Cat 1 Credit. *May 17.* **Geriatrics Seminar.** Info: The Community Hospital at Glen Cove, St Andrews La, Glen Cove, NY 11542. Tel: (516) 676-5000.

May 14. **Clinical Day in Ophthalmology: Orbit and Neuro-Ophthalmology.** 7 Cat 1 Credits. Garden City Hotel. *May 29–30.* **Second Annual Long Island Assembly on Obstetrics and Gynecology: Crisis Issues of the 80s.** 16 Cat 1 Credits. Garden City Hotel. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

May 16. **Selected Topics in Neurology.** 6 Cat 1 Credits. Info: Bernard W. Berkowitz, MD, Department of Neurology, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-3107.

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(*Continued on p 17A*)

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- ***Proven efficacy when used alone in angina[1,4-6]***
- ***Compatible with both beta-blockers and nitrates[7]***

Please see brief summary of prescribing information on the next page.

CARDIZEM® 60 mg tid or qid

diltiazem HCl/Marion

FEWER SIDE EFFECTS IN ANTIANGINAL THERAPY

BRIEF SUMMARY

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist).

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM (diltiazem hydrochloride) in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity
Other:	Polyuria, nocturia.

The following additional experiences have been noted.

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered.

Bradycardia	Administer atropine (0.6D to 1.D mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 36D mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 18D to 24D mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** — CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

CARDIZEM 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other. Issued 4/1/84

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COMMENTARIES

The Peer Review Organization

The Peer Review Organization (PRO) has been functioning for more than one year. This program replaced the Professional Standards Review Organization (PSRO) that had been in existence since 1972, a long life measured against most government programs. The PSRO program was an attempt by Congress to control the escalating costs of the Medicare and Medicaid programs that had been enacted in 1965. The responsibility for review of admissions and hospital stays had been delegated to hospital Utilization Review (UR) committees. This proved to be less than successful. There were many reasons for the failure, including a lack of objectivity by hospital staff members reviewing the performance of their colleagues in the same hospital, time constraints, absence of norms of care, lack of authority to bar payment to abusers, and no coordination between Medicare and Medicaid. Senator Wallace Bennett of Utah pointed out in 1969 that if the program continued under the present concept of UR monitoring, a $240 billion cost overrun could be expected by 1990!

Congress created the PSRO as an amendment to the Social Security Act in 1972. It was a remarkable concept since it was an example of the government working hand-in-hand with the private sector to control costs and assure quality of care for federally-financed sick people. Physicians were given the key role in decision making concerning admissions, length of stay, professional acceptability of care, and appropriate locus of care (eg, hospital, hospice, nursing home).

The PSRO engendered considerable opposition among physicians who resented government intrusion and thought that it was not possible to quantify quality of care. Opposition also occurred among patients who were subjected to shortened stays and in some cases denied admission and payment; hospital administrators who contended with empty beds and less money; and politicians who said that physicians could not police themselves, that they were not cost effective, and that they practiced defensive medicine. Peer review, however, did come to be accepted, although it is unlikely that there would be much quality control in medicine today had it not been for the birth of the Medicare-Medicaid programs. The PSRO program demonstrated a striking impact in health cost management although there was uneven performance by individual PSROs and little support from several federal agencies. Congress, which measures quality in terms of the number of physician and hospital sanctions, was convinced that a more austere program was needed particularly as the Medicare prospective payment system (PPS) began to function. It seems reasonable to conclude that the performance of the good PSROs did have enough impact to foster a new peer review version, the PRO.

Physicians learned from the PSRO experience that it is difficult to work with the federal government due to the constant modification of program requirements and funding. They learned that review systems are not going to go away and that good performance is not always rewarded. It certainly became clear that the medical profession must maintain the major voice in peer review and that judgement about acceptable medical care may only be made by a physician.

The most startling discovery as a result of the PSRO was that there are extreme variations in admissions, length of stay, and cost for Medicare enrollees among similar hospital markets in the United States. Wennberg and Gittelsohn have shown, for example, that Medicare reimbursements for hospitalizations of the elderly were 74% higher in Boston than in New Haven, CT, even though there was no discernible difference in the quality of care.[1] In Iowa, one of the three most populous hospital markets admits elderly patients at a rate that is only 66% of the state average. The chance of having a prostatectomy var-

ied from less than 10% to more than 50% for males by age 85, depending on the place of residence.[1] Also, small area analysis studies in Maine pointed out that area variations for women having hysterectomies by age 70 varied from 20% to 70%. Great variations in the incidence of tonsillectomy and adenoidectomy, hernia repair, transurethral resection, and hemorrhoidectomy have also been demonstrated. These variations clearly indicate an absence of medical consensus regarding the appropriateness and methodology of disease treatment. No one advocates that there is only one way to treat any given disease process. What is desirable, however, are valid variations reflecting sound medical judgement based on a thorough analysis of the outcomes of treatment alternatives. The results of these studies should be transmitted to communities and to hospital medical staffs.

The question is often asked how the PRO program differs from its predecessor, the PSRO? There are several major differences between the PSRO and PRO programs. The latter is essentially a mail order operation associated with the burden of hospital record duplication and mail service delays. On-site review, concurrent review, hospital delegation, and area wide quality review studies have been abandoned. There is an increased emphasis on stellar performance by hospital UR committees and conditions for confrontations between medical staff and hospital administration are present. The PSRO concentrated on length of stay review, whereas under the PPS system, this is no longer necessary with the PRO focusing on admissions. PSROs did little private review, while the PROs are urged to enter this arena and are mandated to conduct such reviews, if requested. The PRO is responsible for validating DRG coding, for certifying the medical necessity of outliers (patients with extremely long hospital stays or expending an unusually large amount of resources), and for a hospital's decision to discharge a patient if medically warranted.

Quality of care has been addressed by a contractual agreement to concentrate on a selected number of surgical and medical quality objectives. These have already been shown to be restrictive, unimaginative, and lacking any baseline data that may even validate that quality problems exist. It now appears that these targets will be abandoned and replaced by the application of generic screens for every case reviewed retrospectively by PROs. The criteria must be appropriate nationally for comparative purposes and flexible enough for regional and local variation. Examples of such criteria might include deaths, transfers from a general care unit to a special care unit, and unplanned returns to the operating room.

The Health Care Financing Administration (HCFA) is currently supportive of efforts on documentation, feedback, and analysis of medical practice variations of the Wennberg and Gittelsohn methodology; these are to be at the discretion of the local PRO. With the great emphasis on a reduction in admissions and a shift towards outpatient and ambulatory care procedures, some individuals think that the scope of the PRO is too narrow. The more hospital care is constricted, the more ambulatory facilities will grow. Many physicians offices are already beginning to look like acute care facilities. It is apparent that the PRO must address this problem. Some notion of possible outpatient care deficiencies might be gained from reviewing all hospital admissions for ruptured appendicitis, diabetic ketoacidosis, gangrene, cellulitis, invasive carcinoma of the cervix, perforated ulcers, digitalis toxicity, and hypertensive crises. Certainly this review would also identify patient delay, lack of cooperation, and failure of patient education.

The American Medical Peer Review Association (AMPRA) has recommended the development of a preprocedure review to protect against overutilization in the outpatient setting and, more importantly, to assure that patients needing inpatient care are, in fact, admitted to a hospital. The AMPRA has also urged Congress to fund a concerted research effort into the definition, measurement, and study of patient outcomes. The Medicare program has expressed a long range interest in capitation systems and has created strong inducements for Health Maintenance Organizations (HMOs) to enroll Medicare beneficiaries. The AMPRA is accordingly supportive of PRO review of HMOs, outpatient surgery, skilled nursing facilities including swing beds, and home health care services. Of concern to all physicians is the fact that under the DRG classification there is no reimbursement system for necessary admissions based on the patient's social need for observation in a controlled environment. There are many Medicare patients who do not meet the current definition of medical necessity but require hospital admission since they may live alone, live a distance from the hospital, or lack social support structures. This poses problems for caring physicians who handle the chronically ill patients left in emergency rooms (ERs) by unsupportive and demanding families. The creation of an additional DRG for these cases would increase respect for the PRO by physicians, lessen their worries about litigation, gain the respect of patients for the Medicare program, and demonstrate that holistic care of the patient is a valid concept. This DRG could conceivably pay a low reimbursement to the hospital for these patients since there is little resource consumption—the amount could be in the $100 to $200 range. This proposal has the strong backing of the AMPRA.

In summary, the PRO is a new program whose performance has not yet been fully evaluated and is one that is working within a different payment system. This program has great potential and will be attractive to physicians as long as the patient is given priority. It must be cost effective, aggressively pursue quality care, and treat both the providers and the consumers with flexibility and sensitivity. The program will most certainly fail if it is subjected to increasing tasks without adequate funding and if the standards used for its evaluation are unreasonable. This could potentially be a instrument designed to destroy the program. In a sense, the PROs must be Medicare's "Good Housekeeping Seal of Approval."

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The role of bronchoalveolar lavage in the diagnosis of pulmonary toxoplasmosis

The protozoan parasite, *Toxoplasma gondii*, may be responsible for fatal disease in immunologically compromised patients in marked contrast to the infection it causes in normal hosts.[1] Central nervous system (CNS) involvement, including meningoencephalitis, has been recognized as the predominant manifestation of toxoplasmosis in this group of patients.[2] Myositis and myocarditis may also occur, although rarely.[1]

Stringent criteria are required for the diagnosis of acute toxoplasmosis. Serologic tests for specific toxoplasma antibodies are the primary method of diagnosis.[1] Acute infections in patients are apparent with a single high IgM indirect fluorescent-antibody titer or a serial two-tube rise in any serologic test.[1] The presence of *T. gondii* in body secretions or tissue, in two of its three forms, makes the diagnosis definitive. Antemortem diagnosis, however, has not been easily accomplished by demonstrating parasites in tissue or secretions with any regularity. A reason for this is that the diagnosis has not been considered with sufficient frequency in immunosuppressed patients.[2] However, it is well known that antemortem seronegativity or negative tissue biopsy results have often been found in postmortem proven cases of toxoplasmosis.[3,4]

Pulmonary toxoplasmosis is an unusual lung disorder that is often seen in immunodeficient patients.[5,6] This form of the disease can be devastating, presenting as acute interstitial pneumonia or as a superinfection in areas of diffuse bacterial bronchopneumonia. As with systemic toxoplasmosis, antemortem diagnosis of this aggressive pulmonary disorder is often difficult.[7] Thus the demonstration of *T. gondii* trophozoites in bronchoalveolar lavage (BAL) fluid by Maguire and associates in this issue of the *Journal* is noteworthy.[8] Indeed, investigators have recently reported the diagnostic yield and safety of various invasive pulmonary procedures in immunoincompetent patients with diffuse infiltrates. BAL alone, or in combination with transbronchial biopsy, appears to be the initial procedure of choice.[9,10]

Bronchoalveolar lavage has a wide spectrum of applicability in the diagnosis and management of interstitial lung disease.[11] One of the first reports of its value in the diagnosis of opportunistic infection in the lung appeared only three years ago.[12] This technique of sampling cells and secretions in distal airways is usually accomplished through a flexible fiberoptic bronchoscope with the administration of supplemental oxygen. Up to 500 mL of sterile isotonic saline are instilled in aliquots of 20 to 50 mL, with 50% of the instilled fluid recovered.[13] The procedure takes from 10 to 15 minutes with complications being mainly related to the performance of the bronchoscopic examination. However, caution must be used when studying patients with hyperirritable airways. Those with unstable heart disease should not be candidates for lavage.[14]

Pulmonary toxoplasmosis appears to be a rare disease, particularly when there are no CNS symptoms. It is apparent from the major studies published on diffuse lung disorders in patients with the acquired immunodeficiency syndrome (AIDS) and non-AIDS immunosuppressed patients that despite efforts to identify it, the organism has proven elusive.[3,6,9,10,15,16] Although hematoxylin and eosin assisted by Giemsa stains are preferred for identifying *T. gondii*, Gram-Weigert and Gomori methenamine silver stains may also identify this parasite. Reported studies have used the combination of these stains to rule out toxoplasmosis. Additionally, a personal communication with Dr Diane Stover of Memorial Sloan-Kettering Cancer Center supports this. Autopsy examination of patients with AIDS having CNS toxoplasmosis, and non-AIDS immunosuppressed patients with fatal illness, have failed to disclose *T. gondii* in the lungs with Gram-Weigert and hematoxylin and eosin stains.[10] Thus pulmonary involvement due to this protozoan parasite would seem to be somewhat unusual.

An interesting aspect of *T. gondii* infection of the lung is that it frequently coexists with another organism.[2,17,18] Theologides and Lee reported that *T. gondii* was part of a multiple infection that included two of the major pulmonary pathogens seen today in the affected AIDS population, *Pneumocystis carinii* and cytomegalovirus (CMV).[18] Since these two pathogens often coexist in patients with AIDS, perhaps the simultaneous occurrence of *T. gondii* is more frequent than had been thought. It may be that it is being missed by the nonspecific staining techniques that exclude Giemsa. Indeed, CMV has been demonstrated as the principal pulmonary co-pathogen of *T. gondii*.[19] Thus it is of considerable interest that the patient reported by Maguire and colleagues died with a lung infection that included both CMV and *T. gondii*.[8]

In conclusion, the report by Maguire and coworkers[8] does not open a Pandora's box, but rather provides valuable information and food for thought. Fluid obtained by BAL may be safely studied antemortem to identify *T. gondii*, an organism that has traditionally proven elusive to diagnose. Finally, since *T. gondii* is often part of a poly-

microbial infection, the frequency of pulmonary involvement with it may be greater than the sensitivity of the present techniques to detect it. Accordingly, we may just have to try harder in order to find it.

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Cancer genetics: strategies for preventive oncology

Advances in cancer genetics have accelerated during the past two decades,[1-3] leading to hereditary cancer syndrome identification among such common sites as the breast,[4] colon,[5] skin,[6] and those areas associated with a large number of mendelian inherited disorders.[7]

In spite of prodigious worldwide documentation of the importance of primary genetic factors in the etiology of cancer, only limited application of this knowledge toward cancer prevention has taken place in clinical practice.[2,5] For example, the compilation of family history for cancer remains neglected in the work-up of patients,[8] and physicians frequently fail to consider the natural history of hereditary cancer in their surveillance of patients at risk. This shortcoming is perhaps a product of the traditional medical education emphasis on environmental factors as being the sole cause of cancer and the restriction of medical attention to a single patient, to the total neglect of potential relatives at risk for cancer.

Only a fraction of patients exposed to any given carcinogen develop cancer. Why is it then that so many patients with heavy carcinogenic exposure remain cancer-free? A plausible explanation is that the genotype controlling cancer expression variably predisposes the host to resistance as well as susceptibility to cancer. This phenomenon has been clearly recognized since the turn of the century at the infrahuman level, and more recently in humans, where an extraordinary inter-human variability in susceptibility to carcinogens has been recognized. These facts are consonant with the concept of ecogenetics.[9] The range of susceptibility to many of the common types of cancer may be as high as 100-fold.[10,11] At the biomolecular level, Harris and associates[11] have shown that binding levels of benzo(a)pyrene to DNA vary from 50- to 100-fold in cultured human cells. This enormous variation in carcinogen interaction with human cells may be attributed to the fact that the majority of chemical carcinogens require enzymatic activation, and herein host factors play a major role in determining variation in such enzyme capability.[12] It has been postulated that the ratio of metabolic activation to deactivation of carcinogens may determine the individual's risk for cancer.[13]

The highest risk for cancer known is that which exists in a patient whose first degree relative manifests cancer in the context of an autosomal dominantly inherited cancer

syndrome.[2] Clinicians must therefore capitalize heavily on genetic clues when evaluating patients and their families. Such clues are embodied in the natural history of hereditary cancer, which differs strikingly from its sporadic counterpart, and is characterized by a significantly early age of cancer onset, an excess of multiple primary cancer, occasional premonitory clinical signs (multiple adenomatous polyps in familial multiple adenomatous polyposis coli) or biochemical markers (calcitonin excess in multiple endocrine adenomatosis, types IIa and IIb), and of specific modes of genetic inheritance within the kindred. This information is of invaluable aid in mounting highly organ-targeted surveillance and management programs.

The study of families with childhood cancer may, in certain circumstances, lead to the recognition of hereditary cancer syndromes that show both childhood and adult onset cancers. A recent example pertained to brain tumors in children where the cancer risk to their adult primary relatives was significantly increased.[14] Birch and colleagues[15] studied the cause of death in the mothers of 143 children with soft tissue sarcomas. Six of these women had premenopausal onset of breast cancer, and two of them had bilateral disease. This represented a three-fold excess risk of breast cancer. Unfortunately, most studies of cancer in children, including the Oxford Survey of Childhood Cancer,[16] have focused almost exclusively on cancers of infancy and childhood, with only limited attention having been given to adult family members.

The observations of Li and Fraumeni[17,18] of soft tissue sarcomas in children, with subsequent attention to their adult relatives, laid the important groundwork for the eventual delineation of a syndrome characterized by *S*arcoma, *B*rain tumors, breast cancer, *L*ung and laryngeal cancer, leukemia, and *A*drenal cortical carcinoma (SBLA syndrome).[19,20] The potential for elucidation of cause and cancer control was revealed in the prospective family studies of this syndrome,[18,20] where syndrome cancers occurred with alarming predictability.

The report by Schreiber and coworkers[21] of an 18-year-old man with a malignant spindle cell tumor of the heart, whose 3-year-old brother died of a metastatic embryonal rhabdomyosarcoma originating in the gluteal region, represents a remarkable familial cancer occurrence. The proband's maternal grandmother had breast cancer. The authors considered the possibility that this case was representative of the SBLA syndrome. The finding of sarcoma primary to the heart, so far as may be determined, would represent the first example of heart involvement in the SBLA syndrome should this family represent this hereditary disease. The mother of the affected siblings in this family may be an obligate gene carrier since her mother manifested breast cancer, which is an integral tumor in the SBLA syndrome. The authors prudently stressed the need for close observation of the family.

How may genetic knowledge expedite cancer control? There are certain strategies that could effectively address this question. 1) Compile a detailed family history and record cancer of all anatomic sites through a minimum of second degree relatives (ie, grandparents, aunts, uncles). These relatives are genetically more informative because of their older ages. 2) Develop appropriate surveillance and management protocols that are responsive to the particular hereditary cancer syndrome's natural history (ie, earlier initiation of highly organ-targeted surveillance, prophylactic subtotal colectomy in multiple adenomatous polyposis coli). Ideally, these protocols should extend to all available relatives at risk for cancer. 3) Establish computerized registries of such kindreds, with capability of dissemination of risk, surveillance, and management knowledge to physicians of all relatives at high risk. 4) Give priority attention to research on biomarkers that correlate with cancer-prone genotypes. 5) Assess reduction in cancer morbidity and mortality in order to influence physician, patient, and societal policy, including demonstration of cost-benefit advantage to third party carriers for defraying the cost of surveillance. All of this will hopefully evolve into a more positive philosophy about cancer prevention.

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The incidence of gestational hypoglycemia in insulin-dependent and non-insulin-dependent diabetic women

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ABSTRACT. The frequency of hypoglycemia was studied in eight insulin-dependent (type 1) and six non-insulin-dependent (type 2) pregnant women with diabetes by capillary blood glucose monitoring. Type 2 women were found to be older and more obese than type 1 women. Mean fasting and postprandial blood glucose levels and glycosylated hemoglobin (HbA_1) levels were similar in the two groups. Hypoglycemia (<60 mg/dL) occurred with significantly greater frequency in women with type 1 diabetes than in women with type 2 (19.2% versus 0.2%; $P < 0.001$). Neonatal outcome was normal for the nine children born thus far. Since the impact of documented gestational hypoglycemia on childhood development has been inadequately studied, prospective developmental studies are therefore planned. Strict control of diabetes during pregnancy is essential although caution is warranted concerning the previously unrecognized potential for hypoglycemia, particularly in women with type 1 diabetes. (NY State J Med 1986; 86:174–177)

The ability to control diabetes has been made possible by devices for capillary blood glucose (CBG) monitoring that are used in conjunction with intensive treatment regimens comprising multiple insulin injections or the insulin pump. These systems of intensive management have been shown to be effective in the treatment of both the nongravid and the pregnant diabetic.[1-19] The principles and application of intensive management regimens have recently been reviewed.[1,3]

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As a result of this modern technology, considerable concern has been expressed regarding the increased potential for hypoglycemia in tightly controlled patients.[7,8,20] Several studies have shown that an inadequate counter-regulatory response to insulin-induced hypoglycemia may be demonstrated in some patients with type 1 diabetes.[21-26] However, this defect may not be present in patients with type 2 diabetes.[26] Several investigators have therefore recommended that insulin-dependent patients who are unable to demonstrate an adequate counter-regulatory hormonal response to insulin-hypoglycemia may be unsuitable for treatment with intensive insulin regimens.[27,28]

The concern regarding hypoglycemia in the intensively treated diabetic population, particularly when the benefit of tight control has not been unequivocally documented, sharply contrasts with the lack of information concerning the occurrence of hypoglycemia in the pregnant diabetic, in whom the benefit of strict metabolic regulation has been adequately demonstrated.[29-31]

Since the frequency with which hypoglycemia occurs in pregnant diabetic women has not been systematically evaluated, a prospective study has been undertaken to determine the incidence of hypoglycemia in intensively managed patients. These data are critical in determining the impact of gestational hypoglycemia on the psychologic and neurologic development of offspring.

PATIENTS AND METHODS

Fourteen pregnant women with diabetes attending the Hi-Risk Center of the New York Medical College/Westchester County Medical Center were enrolled in this study. The patients were classified as either insulin-dependent (type 1) or non-insulin dependent (type 2) according to the following criteria: history

of ketoacidosis; age of onset of diabetes; ideal body weight (IBW); duration of diabetes; and the duration of insulin therapy. Several patients were managed by local physicians subsequent to their referral so that the duration of follow-up was variable.

The women were instructed in CBG monitoring using a reflectance meter. They were asked to perform monitoring at several daily intervals including fasting, one to two hours postprandially, at bedtime, and between 3:00 and 4:00 AM every seven to ten days in order to diagnose asymptomatic nocturnal hypo- or hyperglycemia. Instructions were given for treating hyperglycemia (supplemental regular insulin) and for treating hypoglycemia (eg, 4 to 6 oz orange juice or milk). Target blood glucose values were 80 to 100 mg/dL fasting and less than 120 to 130 mg/dL between one and two hours postprandially. Glycosylated hemoglobin was measured by ion-exchange chromatography (Helena Laboratories, Beaumont, Texas).

The patients were counseled in an ADA exchange diet (30 to 35 kcal/kg) consisting of 40 to 50% carbohydrate, 20 to 25% protein, and 30% fat. The women were asked to test their morning urine samples for ketones and were advised to contact a physician if the results of fingerstick monitoring deviated from the target values or if ketonuria was present. In most cases, insulin was administered as either two or three daily injections of a mixture of short and intermediate-acting insulins (purified pork or human) one half hour before breakfast and again before dinner. If adequate control was not achieved with two daily injections, the evening dose of intermediate-acting insulin was given with a snack at bedtime. The CBG measurements were periodically compared with simultaneous laboratory plasma glucose determinations to evaluate the accuracy of self monitoring.

The mean fasting and postprandial CBG levels were calculated from records kept by each patient. The incidence of hypoglycemia was calculated by dividing the total number of values under 60 mg/dL by the total number of CBG determinations. Ideal body weight was calculated using Metropolitan Life Insurance tables. The means of the variables for type 1 patients were compared with the corresponding means for the type 2 patients by the student's *t*-test. The only exception was in comparing indices of hypoglycemia where a nonparametric randomization was used. Differences were not considered significant when $P > 0.05$.

Results

The characteristics of each patient studied are shown in Table I. Five women were classified as White class B, three as class C, one as class D, two as class F (proteinuria), and two as White class R (proliferative retinopathy). The results of CBG monitoring for type 1 and type 2 patients are shown in Table II.

The differences between women with type 1 and type 2 diabetes are shown in Table II. Women with type 1 diabetes were slender and had a lower IBW than the six patients with type 2 diabetes. Type 1 women were also younger, had diabetes longer, and were treated with insulin longer than those with type 2 diabetes. The mean duration of follow-up was longer for women with type 1 diabetes although this did not reach statistical significance. Type 1 women were found to perform CBG monitoring more frequently than type 2 women. Mean fasting and postprandial CBG levels were similar in type 1 and type 2 women. Mean HbA_1 levels were also similar in both type 1 and 2 women, although the trend tended to be somewhat higher in the type 1 women. Hypoglycemia occurred with significantly greater frequency in type 1 than in type 2 women (19.2% ± 3.1 versus 0.2%; $P < 0.001$). Symptoms of hypoglycemia were not always present; this is consistent with the observation that diabetic patients often have abnormalities in their ability to counterregulate in response to hypoglycemia. The incidence ranged from 0% to 0.7% for type 2 women and from 4.5% to 30.4% for type 1 women.

Eight of the nine children (seven were born to type 1 mothers) had normal perinatal results. Meconium aspiration occurred during one home birth (patient 7) although the baby recovered completely. Patient 9, with type 2 diabetes, had an elevated mean postprandial CBG value and gave birth to a macrosomic infant (4.876 kg). This patient had also performed CBG monitoring less frequently (three times daily) than the other women, and this may have resulted in the higher blood glucose values contributing to the macrosomia.

Discussion

The incidence of gestational hypoglycemia could not be ascertained prior to the advent of CBG monitoring. The present study was therefore initiated to determine the frequency of hypoglycemia in pregnant diabetic women who perform blood glucose monitoring. To our knowledge, the incidence of documented hypoglycemia during pregnancy has not been previously established.

This study demonstrates that hypoglycemia occurred with considerable frequency in type 1 pregnant diabetic women whereas it was essentially absent in type 2 women. The mean incidence of hypoglycemia was 19.2% in insulin-dependent women, ranging from 4.5% to 30.4%, whereas the incidence in non-insulin-dependent women was 0.2%, ranging from 0% to 0.7% ($P < 0.001$).

These findings are consistent with recent observations that patients with type 1 diabetes may be more susceptible to hypoglycemia due to a defective counterregulatory sys-

TABLE I. Characteristics of Patients

Patient	Age	Duration of diabetes	Duration of insulin therapy	White class	Duration of follow-up (wk)	Prepregnancy % IBW
Type 1 diabetic patients						
1	28	25 yr	25 yr	R	31	113%
2	36	24 yr	24 yr	F	31	112%
3	33	25 yr	25 yr	D	24	104%
4	16	6 yr	6 yr	C	10	93%
5	26	15 yr	15 yr	F	32	108%
6	18	16 yr	16 yr	R	10	115%
7	26	3 yr	3 yr	B	4	104%
8	28	25 yr	25 yr	R	3	114%
Type 2 diabetic patients						
9	38	3 yr	1 yr	B	24	101%
10	29	14 yr	9 yr	C	11	179%
11	30	5 yr	2 mo	B	9	208%
12	35	4 mo	4 mo	B	11	201%
13	35	14 yr	5 yr	C	4	167%
14	38	2 mo	2 mo	B	6	163%

Table II. Characteristics of Patients by Type of Diabetes

	Type 1 (n = 8)	Type 2 (n = 6)
Mean fasting CBG (mg/dL)	109.3 ± 8.4	105.8 ± 4.3 (P = NS)*
Mean postprandial CBG (mg/dL)	114.8 ± 3.4	124.7 ± 4.6 (P = NS)
Mean hemoglobin (%)	8.1 ± 0.7	6.8 ± 0.3 (P = NS)
Incidence of hypoglycemia (%)	19.2 ± 3.1	0.2† ($P < 0.001$)
Total number of values	629 ± 200	272 ± 74
Follow-up (wk)	18.1 ± 4.5	10.8 ± 2.9
Mean prepregnancy IBW (%)	107.9 ± 2.6	169.8 ± 15.6 (P = 0.010)
Mean age (yr)	26.4 ± 2.4	34.2 ± 1.6 ($P < 0.05$)
Mean duration of diabetes (yr)	17.4 ± 3.2	6.0 ± 2.6 ($P < 0.05$)
Mean duration on insulin (yr)	17.4 ± 3.2	2.6 ± 1.5 ($P < 0.01$)

* Differences were not considered significant when $P > 0.05$.
† Standard error was not computed; significance determined by nonparametric randomization.

tem than type 2 diabetics who have a normal hormonal response to insulin hypoglycemia.[21-28] Thus the need to achieve physiologically lower blood glucose levels in insulin-dependent pregnant women may predispose to hypoglycemia. The insulin-dependent women in this study had long-standing diabetes (mean duration, 17.4 ± 3.2 years) with microvascular complications present in five patients, whereas the type 2 women had a shorter duration of diabetes (6.0 ± 2.6 years) and no notable complications. These differences are reflected in the White classification of patients and by the significant difference in the incidence of hypoglycemia between type 1 and type 2 patients (Table 2).

The beneficial effect of strict metabolic regulation in the pregnant diabetic has been well documented. A reduction in infant morbidity and mortality may be achieved when diabetes is well controlled throughout pregnancy.[29-31] The incidence of congenital malformations, which occur more frequently in the diabetic pregnancy than in the general population, may be dramatically reduced when diabetic mothers are well controlled prior to conception and before critical organogenesis has occurred early in the first trimester.[32] Control of diabetes needs to be rigorous, and near-normalization of blood glucose levels must be achieved to attain these results. Target blood glucose levels are physiologically lower during pregnancy than in the nongravid state, which makes this goal even more challenging in the insulin-treated diabetic woman.[33] The strictness of these criteria imply that gestational diabetics who do not maintain fasting blood glucose levels under 105 mg/dL with diet alone need to be started on insulin therapy.[34]

Since the desired blood glucose values are lower during pregnancy, it might be anticipated that hypoglycemia would be frequent. Several studies investigating the effect of strict metabolic control on the outcome of diabetic pregnancies have not commented on the occurrence of hypoglycemia.[35-43] Studies that allude to hypoglycemia do not indicate its frequency or provide individual blood glucose values.[16,44-52]

The overall incidence of hypoglycemia is reported in only two studies.[51,52] Rudolf and associates found that 6% of all CBG determinations performed at home by patients treated with insulin pump therapy were under 45 mg/dL.[48] Skyler and colleagues reported that 11% of all mean fasting glucose levels studied fell below 60 mg/dL.[49]

It is likely that the risk of hypoglycemia has previously not been fully appreciated due to the enthusiasm surrounding the desirable results achieved with excellent metabolic control. The paucity of information concerning gestational hypoglycemia contrasts with the visible concern pertaining to hypoglycemia in the nongravid state. This may result from the uncertain effects of hypoglycemia on the mother or the fetus on the one hand, and the well-documented, potentially pejorative effects of hyperglycemia on the other hand.

The considerable frequency of gestational hypoglycemia demonstrated in the present study may be of importance since its impact on fetal maturation and ultimate effect on childhood psychologic and neurologic development have been inadequately studied. Prospective studies of the effects of documented maternal hypoglycemia on offspring are therefore needed. Strict metabolic control remains essential to assure an optimal perinatal outcome although additional information will be required before concluding that hypoglycemia is not harmful. Concern regarding hypoglycemia should therefore extend to pregnancy, as in the nonpregnant state, until further information becomes available.

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DIABETES AND AN OBSTETRICAL AND GYNECOLOGICAL PROBLEM

To the Internist Insulin has removed practically the dreaded coma, and likewise it has enabled the Internist to help the surgeon and the gynecologist and the obstetrician to carry these diabetics with surgical and obstetrical conditions through their operations or deliveries with comparatively little likelihood of this dangerous and fatal complication developing.

Without the medical man, trained in the handling of the dietary treatment of diabetics and familiar with the use of Insulin, however, good surgical, obstetrical and gynecological results in cases with diabetics will not be obtained. There are too many pitfalls into which the surgeon may be led by the diabetic case without his becoming cognizant of the fact at all, and a fatal coma may precipitate itself in a very brief space of time. Close co-operation, therefore, between the medical man and the specialist is most important.

What future possibilities Insulin offers one cannot predict, for the work done so far is but the beginning of a tremendous amount of practical and scientific study which is to be crystallized out in the next few years. As yet but comparatively few cases complicating obstetrics and gynecology have been treated with Insulin.

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Autologous and allogeneic bone marrow transplantation

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Bone marrow transplantation (BMT) is an established treatment modality for severe aplastic anemia, acute and chronic leukemias, and severe combined immunodeficiencies.[1-3] Recently the applications for this procedure have been expanded to include lymphomas and other solid neoplastic lesions[4] as well as inherited storage diseases,[5] severe forms of anemia such as thalassemia major or sickle cell disease,[6,7] and diseases of the reticuloendothelial system such as osteopetrosis.[8]

The aim of this review is to summarize current and relevant literature to aid the clinician caring for patients for whom a bone marrow transplant may be a therapeutic option. Techniques and procedures of bone marrow transplantation will be discussed and patients who are eligible for this therapy described. Potential short term and long term complications will also be discussed.

BACKGROUND INFORMATION

The purpose of BMT is to restore the functions of normally proliferating lympho-hemopoietic stem cells to the bone marrow. The donor may be the patient (autologous transplantation), the patient's identical twin (syngeneic transplantation) or a histocompatible donor (allogeneic transplantation), usually a sibling.

Autologous transplants do not require any immunologic testing for determination of histocompatibility. Allogeneic and syngeneic transplants, however, require immunologic compatibility between donor and recipient. This is done by matching the major histocompatibility antigens (MHC), which are best found in lymphocytes and are known as human leukocyte antigens (HLA). Serologically defined antigens are determined by cytotoxicity assays and comprise the class I loci HLA-A, HLA-B, HLA-C, and the class II locus of HLA-DR.[9] By measuring the proliferative response in a one way mixed lymphocyte culture (MLC), class II antigens—known as HLA-D—are determined.[9] HLA identity and MLC nonresponsiveness are, for the most part, required for successful allogeneic transplants, and there is at least a 25% (usually 30 to 40%) probability of such an occurrence in children of the same biological parents.[1] Donor-recipient ABO incompatibility does not contraindicate transplant and may be managed by several methods.[10] For allogeneic BMT there is an increase in mortality with age. Therefore, some centers will not accept patients over the age of forty.

HARVEST AND INFUSION OF BONE MARROW

For patients undergoing autologous transplantation, bone marrow is aspirated from both iliac crests in small aliquots (2 to 5 mL), anticoagulated with a heparin solution, filtered to remove bone and fat particles, and stored in blood bags. The bone marrow is then refrigerated at 4°C for two to three days while cytoreductive therapy is being administered. After that time the bone marrow is reinfused intravenously similar to that of a blood transfusion.[11,12] Some institutions use cryopreservation in liquid nitrogen at −196°C to store bone marrow for up to several years prior to autologous BMT.[4]

For allogeneic or syngeneic BMT a similar procedure is employed, using strict aseptic conditions under light general anesthesia. The amount of bone marrow mixed with blood that is aspirated varies but is on the average 750 mL and includes about 2 to 5 $\times 10^8$ nucleated cells/kg of recipient. Transfusion of autologous blood to the donor during the harvest procedure facilitates hematological recovery that occurs within a few weeks. The complications resulting from bone marrow aspiration are infrequent and are not serious.[13,14] Donors are usually discharged within one to two days after the marrow harvest.

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Transplant Center

Commitment by an institution to perform bone marrow transplantation requires full cooperation of a transplant team and various subspecialties: a laboratory experienced in tissue typing to perform the HLA and MLC tests for all the members of the family; an on-site blood bank capable of providing large numbers of blood components including single donor and HLA matched platelets; an infectious disease service with experience in the diagnosis and management of immunocompromised patients; support from the clinical chemistry, microbiology, and anatomic pathology laboratories; and a radiotherapy service that can provide accurate dosimetry and shielding for irradiation.

A special care unit should serve as the core of a BMT center. Patients should be admitted to the unit a few days before the beginning of chemotherapy and radiation therapy. All patients should have central venous access lines and be managed in a positive pressure HEPA-filtered room in a reverse isolation system. Parenteral nutrition, antibiotics, and blood product support are needed until hemopoietic recovery ensues. The conditioning regimen varies with each specific disease and will be approached in relation to each clinical entity.

Physical, psychological, and occupational therapies must be provided for the patients throughout their hospital stay. Family support plays a large role in dealing with daily changes and continuous stresses, and support for the family should be provided by the transplant team as well as by friends and relatives.

Bone marrow transplantation is a costly procedure, and is currently estimated in excess of $50,000 for allogeneic BMT in the United States. While third party providers cover most of the costs of this procedure, several extra expenses often remain a burden for families. Autologous transplantation involves less risk overall, is less expensive, and has a shorter in-hospital stay.

Clinical Course

The clinical course following autologous transplantation is usually short with hematological recovery occurring within nine to 18 days. After the marrow harvesting the patient is given combination chemotherapy and radiation therapy to eradicate the neoplasm. During this period the patients are at high risk for infection and bleeding. Failure of engraftment is rare, and there is no graft rejection. The results of the autologous transplants performed at our institution are summarized in Table I.

The clinical course following allogeneic grafting is far more complex.[1-3] The patient is conditioned with some form of immunosuppressive and ablative therapy, usually a very high dose of cyclophosphamide, with or without total body irradiation (TBI). This has several effects: the tumor and the host's marrow are ablated and their lymphoid tissue is largely destroyed. This therapy is usually lethal if not followed by allogeneic marrow grafting. Despite the remarkable cytocidal activities of this therapy, failure of engraftment, graft rejection, and graft versus host disease (GVHD) still occur, all of which may adversely affect the outcome of BMT.

The results of allogeneic BMT at New York Medical College for various hematologic syndromes are detailed in Table II. These patients are usually immunosuppressed for longer periods of time and thus are at an increased risk for infection or hemorrhage. Acute GVHD occurs in about 50 to 70% of all patients, may present at any time within 100 days after BMT, and primarily involves the skin, bowel, and liver.[1-3] The signs and symptoms may be nonspecific, such as rash, diarrhea, cholestasis, and require aggressive work-up and pathological examination of appropriate biopsy specimens. Chronic GVHD may follow acute GVHD or arise de novo, occurring three months to two years after transplant. It resembles autoimmune collagen-vascular disorders and often results in prolonged

TABLE I. Autologous Bone Marrow Transplantation

Diagnosis/ stage*	No	Age	Sex	Pretransplant therapy†	Clinical status
HD-resistant	6	27	3M 3F	VP16 + CTX ± BCNU	Two patients had complete remission at one and two mos; one had partial response at eight mos; one patient had no response; one had complete remission at three mos (which then progressed and led to death); and one patient was too early to evaluate.
NHL-resistant	5	25	3M 2F	VP16 + CTX ± BCNU	Three patients had partial response (one died at two mos from pneumonia, one died from progression of disease, and one died from Aspergillus); one patient had no response; and one was too early to evaluate.
Ovarian cancer	1	38	F	VP16 + CTX	Patient died from Candida sepsis.

* HD: Hodgkin's disease; must have failed at least MOPP, ABVD, and radiation; NHL: non-Hodgkin's lymphoma; must have failed at least two to three aggressive protocols.
† VP16: etoposide 1,800 mg/m^2; CTX: cyclophosphamide 120 mg/kg × 1; given prior to bone marrow harvesting; BCNU: carmustine 600 mg/m^2; given prior to bone marrow harvesting; BM: autologous, untreated, refrigerated (2 to 6°C); given prior to bone marrow harvesting.

immunosuppression that is worsened by the administration of immunosuppressive agents such as azathioprine and prednisone. Severe, debilitating, chronic GVHD occurs in less than 5% of all patients.[2,15]

Prophylaxis of acute GVHD has been achieved by methotrexate or cyclosporin A. At our institution cyclosporin is routinely used with careful monitoring of renal function. Neither cyclosporin nor methotrexate is of benefit for chronic GVHD, nor will they alter preestablished acute GVHD.[2,15]

For patients undergoing syngeneic BMT, no GVHD prophylaxis is required and these patients tend to have a less complicated hospital course. Paradoxically graft- versus host-like reactions have been reported in some patients after syngeneic grafting,[16] which raises interesting questions regarding the cause and pathogenesis of GVHD.

Recent observations on leukemic cell relapse in this group of patients, as compared with patients receiving allogeneic transplants, have suggested a protective role of a graft-versus-leukemia component of GVHD.[17] However, this remains controversial and studies in progress are challenging this concept.[18]

There are data available that document an increased mortality for patients beyond the third decade undergoing BMT. These data apply to aplastic anemia and leukemia and are primarily due to a higher incidence of early infection-related deaths.[3] These deaths are due to many factors that include more severe GVHD, worsened by the administration of immunosuppressive agents, and prior exposure to cytomegalovirus (CMV) and herpes viruses. Although there has been mention of deficient thymus function in older individuals there are currently no substantive data available on the value of thymus hormone replacement in these patients. Improved approaches at controlling or preventing GVHD, the use of CMV-negative blood products, and the prophylactic use of acyclovir[19] may all eventually contribute to an improved survival for these older (ie, third and fourth decade) patients.

Clinical Applications of BMT

Severe immunodeficiencies. This category represents a heterogeneous group of children with variable cellular and humoral immune deficits and usually a limited life span unless treated by transplantation.[3,20] For patients with severe combined immunodeficiency (SCID), transplantation should be performed as soon as possible and does not require prior immunosuppression. For the other immunodeficiencies such as Wiskott-Aldrich, Chediak-Higashi, and Kostman syndromes, BMT requires a pretransplant immunosuppressive regime to avoid graft rejection.[3]

Storage diseases and osteopetrosis. Inherited storage diseases usually result in multi-organ failure and early mortality for patients with severe forms of these diseases. Bone marrow transplantation has been attempted successfully for various mucopolysaccharidosis with clinical and biochemical improvement.[3,5] However, it is unlikely that BMT will correct the severe neurologic dysfunction in some of these diseases.

Osteopetrosis results from impaired osteoclast function. Bone marrow transplantation has been successful for four of five patients with this condition, which also suggests that osteoclasts arise from hemopoietic stem cells, presumably from the monocytic lineage.[8]

Congenital anemias. Bone marrow transplantation has been attempted in cases of thalassemia major,[6] Fanconi's anemia,[21] in patients with Diamond-Blackfan syndrome,[22] and in one patient with sickle cell anemia and acute leukemia.[7] The results have been positive overall. However, the high morbidity and mortality of this procedure necessitates critical selection of patients with severe forms of these diseases for BMT.

Aplastic anemia. The studies by Camitta and associates[23] established the superiority of bone marrow transplantation over conventional modalities of treatment for patients with severe aplastic anemia (SAA). The clinician caring for these patients should offer the option of transplantation early in the course of the disease. These patients have a lesser incidence of graft rejection and a more benign post transplant course. Patients with SAA are often quite ill at the time of referral for BMT, in contrast to patients with leukemia in remission or in chronic phase who are usually in good clinical condition. Patients with SAA should not be transfused with blood products from family members, unless a BMT has been ruled out, since they will likely result in failure of engraftment even with more intensive immunosuppressive therapy.

The earlier studies show the high incidence of graft rejection that correlated with a history of multiple transfusions.[24] The recent additions of more intensive immunosuppressive regimens—total lymphoid irradiation, low dose total body irradiation, and cyclosporin—have resulted in a 70% long term survival for patients with HLA-matched siblings because of a lowered incidence of rejection in sensitized patients.[25,26] For patients without matched donors the use of antilymphocyte or antithymocyte globulin has steadily gained acceptance, especially considering the 50% long term recovery rate for treated patients.[27] These trials were based on several laboratory investigations demonstrating an immune mediated suppressor-type mechanism in a subset of patients with idiopathic aplastic anemia.[28,29] The current protocol involves the use of cyclophosphamide 50 mg/kg for four days with or without radiation for sensitized or unsensitized patients. Of interest is the hematological engraftment in two patients with busulfan-induced aplasia,[30] suggesting that even though marrow stroma is damaged by the chemotherapy it is still able to provide a home for the normal donor's bone marrow cells.

Chronic granulocytic leukemia. The therapy for chronic granulocytic leukemia (CGL) has not changed in the past 20 years.[31] It does not prolong survival or eradicate the Philadelphia (Ph) chromosome, and so this disease —which accounts for about 25% of leukemias in adults —still has a short median survival of three years.[31,32] Bone marrow transplantation has been used for patients with blastic crisis, following remission induction of blastic crisis, for accelerated CGL, and more recently for chronic phase CGL.[1-3,31] Attempts at BMT for the first two stages of CGL have met with little success (10 to 20% long term disease-free survivors). More recently BMT for accelerated or chronic phase CGL is reported to provide about 50% long term disease-free survivorship. Of particular interest are the reports showing resolution of concurrent myelofibrosis in patients who engrafted.[33] Also of note is

TABLE II. Allogeneic Bone Marrow Transplantation

Diagnosis/ stage*	Pretransplant No	Pretransplant Age	Pretransplant Sex	Pretransplant therapy†	GVHD	Clinical status
CGL (chronic aplastic blastic phase)	2 2 1	26 28 34	1M/1F M M	CTX/TBI	0	All died from interstitial pneumonitis and sepsis; no evidence of CGL.
AML (remission relapse)	4 2	33 21	M 1M/1F	CTX/TBI	I–II Skin	Alive with no evidence of disease at 2 to 14 mos.
AA (severe post-ATG)	1	34	M	CTX/TLI	0	Day +30; engrafted
MDS	1	46	M	CTX/TBI	II-GF	Alive with no evidence of disease at 3 mos.
FELH (relapse)	1	1	M	CTX/TBI	0	Died; sepsis with positive disease at autopsy.

* CGL: chronic granulocytic leukemia; AML: acute myelogenous leukemia; AA: aplastic anemia; MDS: myelodysplastic syndrome; myelofibrosis; FELH: familial erythrophagocytic lymphohistocytic syndrome.

† CTX/TBI: cyclophosphamide 60 mg/kg × 2, total body irradiation 120 rad × 10 in 5 days; CTX/TLI: cyclophosphamide 50 mg/kg × 4, total lymphoid (nodal) irradiation 750 rad × 1 day.

the occasional chimeric state seen after BMT with temporary persistence of the Ph chromosome in recipient cells that then spontaneously disappear.[34,35]

Pretransplant splenectomy has no effect on outcome of BMT.[36] Some recent studies now suggest that BMT in the first year of the disease improves the survival as compared to patients transplanted in the second and third year, particularly if the patients are treated with busulfan. These results do not seem to apply to patients treated with hydroxyurea. Patients with poor prognosis features, such as Ph-negative CGL, extra cytogenetic abnormalities, and progressive disease, are usually advised to be typed and transplanted early in the course of their disease.

Autologous bone marrow transplantation has been used for rescue of patients treated with aggressive chemotherapy for blastic phase CGL. These patients enter a new chronic phase of the disease and this modality of therapy has provided only short-term prolongation of survival.[37]

Acute leukemia. The indications for marrow transplantation vary with the type of leukemia and with the patient's age.

Childhood acute lymphocytic leukemia (ALL) is the most common malignancy in this group and is usually treated with aggressive combination chemotherapy with excellent results (overall long-term survival greater than 50%).[38–40] Because of good first remission prognosis bone marrow transplantation is recommended only for patients who relapse and achieve a second remission. Attempts at transplantation during relapse showed a high incidence of recurrent leukemia with survival being less than 20%.[3] Chemotherapy with cyclophosphamide (60 mg/kg × 2) and hyperfractionated TBI (1,200 rad), is the standard pretransplant conditioning regimen, but care should be taken to avoid excessive cranial irradiation in patients who have had radiation therapy to prevent CNS leukemia. In patients for whom BMT is a consideration cranial irradiation should be limited to 1,800 rad,[41] or if the patient is to be transplanted soon, CNS prophylaxis should be limited to methotrexate. Overall survival for this group of patients is about 35%, due to a high incidence of recurrence of the leukemia, in some cases in donor cells.[42,43] Some recent studies have addressed the issue of BMT for patients in first remission, particularly those for whom prognostic indicators are poor, such as patients with B-cell ALL, those presenting initially with high white blood cell counts, prolonged induction therapy (greater than 28 days to complete remission), and those with certain cytogenetic abnormalities (9:22, 1:19, 4:11 translocations).[39]

Response to chemotherapy in patients with adult ALL has also been good, with a 40% incidence of long term disease-free survival.[44–46] However, as with childhood ALL the results with BMT in relapse are not good. Bone marrow transplantation has been used for patients in second remission with similar survival rates.[1,3] There are recent attempts to improve the pretransplant conditioning regimen by the addition of other chemotherapeutic agents such as cytosine arabinoside.[47] It is still too early to predict whether these will have the expected benefit by decreasing the leukemic relapse rate.

With current therapy the remission rate for childhood acute nonlymphocytic leukemia (ANLL) is about 60 to 70%, but only about 25% have a continued remission of more than two years,[48,49] although there are reports of higher (50%) continued remission rates.[50] The disease-free survival rate for young patients transplanted in first remission is 60 to 80%. For patients in a second or greater remission the rates decrease to 34%, but these are still much better than results with chemotherapy alone. The Children's Cancer Study Group sponsored a prospective randomized trial comparing BMT to conventional chemotherapy; this should be able to clarify the role of BMT in first remission childhood ANLL.

Concerning adult ANLL, BMT has been limited to individuals less than 50 years of age. The results are similar for childhood ANLL and some recent studies suggest an advantage in disease-free survival for BMT over chemo-

therapy.[51,52] There are also data to support the view that relapse of the leukemic process occurs rarely beyond two years after the marrow transplant, whereas late relapses continue to occur in patients treated with chemotherapy alone.[51,52] Four patients were transplanted in second or greater remission (Table II). All of the patients survived without evidence of disease. Only one patient developed moderate GVHD of the skin; this resolved with high dose oral prednisone therapy. These patients continued to be intensively monitored since they are at a high risk for relapse.

Lymphomas and solid tumors. Allogeneic BMT has been used for some patients with poor-prognosis lymphomas, such as Burkitt's and T-cell lymphoblastic lymphomas, with a 50% disease-free survival rate.[53] For patients with other lymphomas and Hodgkin's disease who have become resistant to conventional chemotherapy autologous marrow rescue has been used in combination with high dose cytotoxic chemotherapy. By improving cryopreservation techniques enough cells may be obtained from one marrow harvest to be used for two or more autologous infusions. Autologous marrow rescue is reserved for patients with disease that is resistant to currently available aggressive chemotherapy and that is without marrow involvement. Such patients have usually been through several induction regimens or have not entered complete remission with any protocol. They should be in good general condition in order to survive this procedure. A major limitation of autologous BMT has been the appearance of significant, sometimes unexpected, toxicity from these supra-lethal doses of chemotherapy. The current protocol involves the use of a combination of 3 drugs: carmustine (BCNU) (600 mg/m^2), cyclophosphamide (120 mg/kg), and etoposide (VP-16) (1,800 mg/m^2) in a single dose. Forty eight hours later refrigerated (2 to 6°C) autologous marrow is infused. A mean of 800 mL of marrow, containing an average of 3.9×10^8 nucleated cells/kg recipient was obtained. Overall response rate is estimated at around 50% but long term disease-free survival will only reach about 10%. Hematological recovery has been rapid and complete in all patients, with a mean time of 8.8 days (WBC greater than 1,000/μL) (Table I).

Similar protocols have been developed for the treatment of other tumors such as small cell lung cancer, germ cell testicular cancer, and ovarian cancer. The results are encouraging, but more studies are needed to validate this form of therapy.[54]

Future Approaches

The therapeutic use of allogeneic bone marrow transplantation is currently limited to a minority of patients with HLA-matched siblings. Several approaches are being actively pursued at our institution and other major institutions that involve the use of unrelated histocompatible donors. The Seattle Transplant Group has just recently updated their experience with mismatched bone marrow transplants.[55] They compared 105 patients receiving haploidentical grafts with 728 HLA genotypically matched transplants. They noted a delay in engraftment, a large increase in marrow graft rejections, and earlier onset of more severe (grade II–IV) GVHD. There was no particular association with the type of HLA mismatch. However, the authors were unable to detect any survival difference between the two groups, and the causes of death were similar for both groups.

The use of T-lymphocyte depleted bone marrow grafts is now being advocated since lymphocytes are thought to be responsible for GVHD in allogeneic BMT, and animal studies have conclusively shown that removal of mature T-cells allows for transplantation across major histocompatibility barriers.[56,57] Removal of T-lymphocytes from bone marrow may be done by physical separation[58] as pioneered by Memorial Sloan-Kettering Cancer Center, or by using monoclonal anti-T lymphocyte antibodies.[59,60] A method for the separation of T-cells from the hemopoietic stem cells by use of continuous elutriation is currently being explored. This technique involves the separation of cells according to size by centrifugation in a specially designed chamber. Recent results using these methods were reported at a meeting of the American Society of Hematology.[61-63] Although these methods are promising, more patients need to be treated with these protocols to determine the efficacy of these approaches. An increase in the numbers of graft rejections and the appearance of malignant lymphomas following transplant are only some of the problems faced by investigators in this field.

Another application of the monoclonal antibody technique is the development of antitumor antibodies for the elimination of tumor cells from autologous bone marrow. This approach has been successful in cases of ALL[64] and is now also being actively pursued for other diseases.

Still in the experimental phase is the development of methods of gene insertion for correction of severe metabolic or biochemical defects. In autologous BMT, besides the use of antitumor antibodies, further work needs to be done to allow more efficient cryopreservation of bone marrow cells, and work will continue on defining toxicity of chemotherapy and radiation therapy regimens. With further advances bone marrow transplantation will become available to even more individuals with a variety of serious illnesses.

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Medicine, adventure, pirates, and castaways

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Tales of adventure have an irresistible attraction. Such stories might have been consigned to a lowly position in literature as mere "boys' books" were it not for the high quality attained by some outstanding exponents of the art. The classic desert island story, *The Life and Adventures of Robinson Crusoe* (1719), by Daniel Defoe (1661 to 1731), has a medical association. The popular portion of this long book with its detailed description of one man's successful struggle to create a passable home, agriculture, and husbandry—unaided and in prolonged solitude—is only part of a much more extensive tale of adventure liberally spiced with primitive theology. When Oliver Goldsmith in *The Vicar of Wakefield* (1766) allows Dr Primrose to doubt his daughter's depth of reading, Olivia includes in her defense the fact that she has read the controversy between Robinson Crusoe and Friday the savage. John Laird, professor of Moral Philosophy at the University of Aberdeen, described *Robinson Crusoe* in 1946 as "a thoroughly philosophical romance" and discussed it at length in this vein.

> There is a convention that desert-island stories are boys' books in some special sense. When the boy is a little too old and a little too critical for the giants and ogres of his fairy-tale years he is promoted to the desert-island class, there to nourish his imagination upon the ingenuity of the castaway and upon the pirates, savages and mutineers who are usually employed either for putting the solitary upon the island or for getting him off.[1]

Rousseau (1712 to 1778) may have been partly responsible for the fame that *Robinson Crusoe* achieved as a children's book for in his novel *Emile* (1762), a serious work on education that influenced Pestalozzi, Defoe's story is Emile's first textbook. Also, Offenbach surprisingly made *Robinson Crusoe* into an operetta.

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Robert Louis Stevenson is another popular adventure story teller (though he was so much more besides). In this field, or perhaps one should say on these seas, *Treasure Island* (1883) rides triumphantly paramount. *The Sea Cook*, which became *Treasure Island*, began as an amusement for a young boy who found his stepfather's books uninteresting, was sorry to see him so unsuccessful, and felt that he ought to do better. Stevenson had published some essays, *An Inland Voyage* (1878) and *Travels with a Donkey* (1879), that had been favorably commented on by George Meredith and Henry James but, up to that time, had never earned more than £200 in a year from his writing. The first half of *Treasure Island* was started one September as family entertainment, with Stevenson's father as well as his stepson[2] becoming rapidly enthralled. They were staying in Braemar at "The Late Miss M'Gregor's Cottage" and Sidney Colvin and Edmund Gosse came on a visit. With nothing much to do but watch the Queen drive by when the rain stopped, they joined the family each afternoon to hear a reading from the chapter of *Treasure Island* written that morning. It was their enthusiasm that secured the transformation of this family entertainment into a famous novel, the second half of which was written that winter in Davos, Switzerland.

Few adventure stories have had a finer start. Nothing could be more suitable or better calculated to set the scene and arouse excited anticipation than the means employed to introduce the map of the island around which the whole story is built. First there is the arrival at the Admiral Benbow of the mysterious Captain with his sea chest, to be followed by blind Pew, tapping his way there to fix the black spot in the palm of the Captain's hand, and then, by the sudden dramatic deaths of both of these old pirates, leaving the vital map in the possession of Jim Hawkins. Throughout the book, brave deeds are set forth in brave words with just that proper balance of foolish mistakes

and good luck on Jim Hawkin's side to keep the reader anxious and to see them through.

There is an admirable doctor present in this story. Throughout the tale this neat acute man with his pleasant manner and bright black eyes never flags in courage or good sense. Dr Livesey, a slave to tobacco, is an old soldier who had served with his Royal Highness the Duke of Cumberland and was wounded when they were defeated by the French at Fontenoy in 1745. He displays his quality from the start. When the pirate Captain inflamed by rum strikes the table and shouts for silence in the Admiral Benbow and then advances on the physician with an open clasp-knife, he is forced by the power of the physician's manner and words alone to resume his seat like a beaten dog. It is the physician to whom Jim goes with the oilskin packet, and it is the physician who cuts the stitches with his medical scissors as he dines with Squire Trelawny on that fateful day when they decide to go treasure hunting. The only sign of anxiety ever displayed by Dr Livesey occurs when he is seen to take off his wig and place it on his lap. On one occasion, at the low ebb of their fortunes on the island when the doctor is admitted under truce to attend the sick and wounded among the mutineers, "he seemed under no apprehension, though he must have known that his life among these treacherous demons depended on a hair." Dr Livesey rattles on to his patients as if he was paying an ordinary professional visit to a quiet English family and feels it to be "a point of honour not to lose a man for the gallows." The "brandy-faced rascal," Israel Hands, who is one of the pirate crew, had a real life namesake, Israel "Basilica" Hands, sailing-master to Captain Edward Teach, known as Blackbeard, who once shot Hands in the knee on the grounds that "if he did not shoot one or two of them now and then they'd forget who he was."

There have not been many physicians who have been genuine pirates—although Coleridge once said "No man is a pirate, unless his contemporaries agree to call him so." There were those who were recruited as medical officers on privateers and some, like Adam Cowry and John Hincher, who were captured by pirates at sea and forced to serve.[3] Peter Scudamore was taken in this manner but took to the life and loot to be won so enthusiastically that he became a true pirate when he signed the articles and was, perhaps, the only physician-pirate to be hanged. Robert Bradinham sailed with Captain Kidd, Richard Browne with Henry Morgan, George Wilson with Bartholomew Roberts (who, being a Welshman, was able to combine strict Sabbatarian views, opposition to gambling, and being teetotal with the activities of a highly successful pirate), John Ballet with William Dampier, Bullock with Captain Sharp, and Lionel Wafer with Captains Cook and Lynch.[3]

There was one literary physician-pirate, Thomas Lodge, educated at Merchant Taylor's School and Trinity College, Oxford, a barrister son of a Lord Mayor of London, who wrote plays, poems, and stories, among which was *Rosalynde* (1590), a source of Shakespeare's *As You Like It*. He began writing poetry in his buccaneering days but did not take up medicine at Avignon until after he had given up piracy. With a fine display of versatility Thomas Lodge then became a successful London physician—perhaps a little poetry and a grand spirit of adventure constitute fair support for such a career.

Peter Blood probably became the best known physician-pirate through the Warner Brothers film of 1935 of Rafael Sabatini's book *Captain Blood: His Odyssey*. The hero was played by Errol Flynn in that grand romantic style of his that made the physician seem so unreal that one came to doubt his authenticity. Dr Blood, a descendent of Martin Frobisher, graduated in medicine from Trinity College, Dublin. However, having a taste for adventure, he went to sea and served under the great Dutch sailor, Admiral de Ruyter, who had brought his ships up the Medway in 1667 to burn the fleet anchored below Rochester. Peter Blood joined him on his last expedition against the French in the Mediterranean. After fighting with the French army, for a change, against the Spanish in the Netherlands, he settled down at the age of 32 to practice medicine in his mother's county of Somerset. He must have created a grand impression with his fine clothes, romantic appearance, Irish brogue, and fluency in several languages. No peaceful life was yet to be his, however. When Monmouth was defeated at the battle of Sedgemoor, Peter Blood, called to attend to a wounded rebel, was arrested at his mission of mercy by the King's dragoons and unjustly convicted of treason. He was sent as a slave to Barbados and sold there to Colonel Bishop. Dr Blood made himself so useful by treating the Colonel's gout and his lady's migraine, and was so pleasing to their niece Arabella that he obtained a privileged place in their household. In 1686 Don Diego de Espinosa y Valdez raided Bridgetown and overpowered the garrison. While they were sacking the city, Peter Blood and other slaves rowed out, captured the ship, and then destroyed the invaders by turning their own guns on the returning crew. Dr Blood and his fellows renamed the ship *Arabella* and joined the Brotherhood of the Coast: sinking Spanish galleons; sacking the city of Maracaibo; and taking two 20-gun frigates and, in one famous action, disposing of two Spanish ships at once by sailing straight betweem them and delivering devastating broadside blows while they hesitated to fire upon each other.

When William of Orange came to the throne in 1689 the French attacked and sank an English ship with Lord Willoughby, the Governor General of the West Indies, on board. However, Captain Blood was on hand to rescue the Governor General's party.[4] Peter Blood finally sacrificed his ship in a daring intervention against a French attack on Port Royal, Jamaica, where, as his ship sank, his men boarded the French vessel and overpowered them in hand-to-hand combat. Lord Willoughby offered Captain Blood the governorship of Jamaica and there he settled down at last to a peaceful life married to Arabella Bishop. The whole story seems far more likely to have been a fictional vehicle for Errol Flynn than the real-life adventures of Dr Peter Blood.

Another famous physician-pirate was Thomas Dover (1662 to 1742), an almost exact contemporary of Daniel Defoe. He took a share in an expedition to attack Spaniards in the South Seas organized by merchant-adventurers of Bristol. Thomas Dover's piratical interlude occurred between two periods of medical practice, first in Bristol and then in London. He was born in Warwickshire

FIGURE 1. Captain Woodes Roger's crew politely stripping Spanish ladies of their jewels at Guiaquil. (Photograph courtesy of the British Broadcasting Company, Hulton Picture Library.)

and received his BA from Oxford and his MB from Cambridge from Gonville and Caius in 1687. When he came back from his voyage—a wealthy man from his share of the booty—Dr Dover saw his patients at the Jerusalem Coffee House in Cecil Street, Strand. In 1732 he wrote *The Ancient Physician's Legacy to his Country*. His faith in the healing power of mercury earned him the name of "The Quicksilver Doctor," and he is still remembered for one of his prescriptions, a diaphoretic containing opium and ipecacuanha known as Dover's Powder.

Thomas Dover's voyage as a privateer was with two ships, the *Duke* of 320 tons, with a crew of 117, and 30 guns, and the *Duchess*, of 260 tons, with a crew of 108, and 26 guns. The latter vessel was commanded by Captain Woodes Rogers of Poole in Dorset who took them around the world and was later appointed Governor of the Bahamas. Dover sailed in the *Duke* with William Dampier, who had led his own expeditions before. Dover was appointed president of the council that controlled most of their activities, especially the distribution of the booty. These pirates set off on their adventure in August 1708, captured vessels large and small, with one rich prize being a ship out of Manila taken off the coast of California; sacked and ransomed Guiaquil, a town in Equador; and arrived back in England on October 1, 1711. Thomas Dover first transferred to the *Duchess* and then to a Spanish prize after a disagreement among the crew because his temper was so violent that capable men could not work under his supervision. However, Thomas Dover sailed back to the Thames as master of the Spanish prize of 21 guns with Alexander Selkirk on board as his first mate.

When rounding Cape Horn in January 1709 the ships had been driven south by a great storm and were directed toward the island of Juan Fernandez on January 31st. A light was seen on land and Thomas Dover took the boat to shore to investigate. There he found and rescued Alexander Selkirk, an old shipmate of William Dampier's and the chief inspiration for Robinson Crusoe, dressed in goatskins who had been marooned alone on the island for four years and four months.

Alexander Selkirk (1676 to 1721) was the seventh son of John Selkirk, a shoemaker of Largo in Fifeshire. He ran away to sea in 1695 after being accused of "indecent conduct in church," returned in 1701, and was off again privateering with William Dampier to the South Seas in 1703. On this voyage he was sailing master in the *Cinque Ports* under Charles Pickering, who died of fever. It was then, when Thomas Stradling took command, that the trouble began.[5] They put into Juan Fernandez and rescued two men found castaway on the island. Stradling and Selkirk must have had a row of grand proportions about whether the ship was fit to sail without more time taken for repairs for Stradling replaced the two men he had rescued from the island with Selkirk, who was left frantically waving from the beach while they sailed away. Selkirk seems to have been both right and lucky, however, for the *Cinque Ports* began to leak and had to be run ashore in Colombia, with many of the crew being killed and the rest captured by the Spaniards. It was over four years before the next ship blown off course arrived at Juan Fernandez, and Dr Thomas Dover came ashore to bring Selkirk back to the *Duke* to be reunited with William Dampier. When rescued Alexander Selkirk's speech failed him "for want of use," he seemed to speak his words in halves, and at first they "could scarce understand him." His triumphant return to England sailing with Thomas Dover on a captured Spanish ship as first mate occurred nearly eight years after he had first been castaway.

Selkirk's subsequent history alone would have made a fine romance. With his share of the booty—some £800 which was a good fortune in 1711, he returned and paid a visit to Largo dressed in fine clothes and gold lace. He arrived on a Sunday to find that his whole family was in church. Entering while the service was in progress all eyes turned to look at this grand figure, once accused of indecent conduct in this place, and recognized at last by his mother who interrupted the proceedings by uttering a

FIGURE 2. Painting of William Dampier by T. Murray, circa 1697–1698. Dampier was the only buccaneer to have his portrait painted. (Photograph courtesy of the National Portrait Gallery, London.)

great cry and rushing down the aisle to embrace him. He stayed a while but then ran off with a quiet local girl, Sophia Bonce, to London, and made a will in her favor. In a few years, however, restless for the sea and with his money running down, Selkirk enlisted in the navy. He then married an attractive widow, Frances Candis, made a new will in her favor and died of yellow fever off the Gold Coast. A battle over his will was fought by Frances, married yet again, who won the case leaving poor Sophia to beg for charity.

It seems unlikely, despite a considerable literature of myth on the subject, that Defoe ever met Alexander Selkirk, his Robinson Crusoe, or any of the other participants in the great adventures of the *Duke* and *Duchess*. Captain Woodes Rogers wrote an entertaining book in 1712 about the voyage and the rescue called *A Cruising Voyage Round the World*.[6] Richard Steele (1672 to 1729) did meet Selkirk and wrote an essay on him in *The Englishman* in 1713 in which he refers to Largo, six years after the union of England and Scotland, as being "in her Majesty's dominions." Other accounts of the rescue of Alexander Selkirk appeared and it was from such works that Defoe obtained material for the first part of *Robinson Crusoe*. The story of a man castaway on a desert-island is a theme of great antiquity. R. L. Mégroz[7] noted that the 12th century story of Hayy ibn Yaqzan by Ibn Tufail, in Arabic, based on an even older tale of a solitary castaway, was translated into English in 1708 and that a study of the book allows little doubt that Defoe had read this philosophic and moral treatise before writing *Robinson Crusoe*. Many authors have adapted this same theme to their own work, including Shakespeare in *The Tempest*.

At least two desert-island stories have been written by physicians: *Child of Ocean* by Sir Ronald Ross (1857 to 1932), the Nobel Prize winner for medicine in 1902, and *The Blue Lagoon* by Henry de Vere Stackpoole (1863 to 1951), based on his experiences in the South Seas.

Defoe's account of Robinson Crusoe's long period of perilous solitude, surmounted with hard work and good luck, is sandwiched into a life of wild and profitable adventure. However, it is this interlude with its practical ingenuity, dry realism, and vague reflections on life and religion that has lasted. Virginia Woolf described Crusoe as a sturdy, middle class man who was forever doing sensible things, making common actions dignified and common objects beautiful. She wrote the following:

> Everything appears as it would appear to that naturally cautious, apprehensive, conventional, and solidly matter-of-fact intelligence. He is incapable of enthusiasm. He has a natural slight distaste for the sublimities of Nature. He suspects even Providence of exaggeration. He is so busy and has such an eye for the main chance that he notices only a tenth part of what is going on around him. Everything is capable of a rational explanation, he is sure, if only he had the time to attend to it.[8]

So we accept extraordinary things that we would have jibbed at if they had been offered to us by an imaginative and flamboyant traveller.

Alexander Selkirk's adventure from which he was rescued by a physician inspired a poem as well as Defoe's famous work of fiction. William Cowper's verse is supposed to have been written by Selkirk on Juan Fernandez and it starts with the following:

> I am monarch of all I survey,
> My right there is none to dispute;
> From the centre all round to the sea,
> I am lord of the fowl and the brute.
> O Solitude! where are the charms
> That sages have seen in thy face?
> Better dwell in the midst of alarms,
> Than reign in this horrible place.[9]

There were many occasions when, back in his own country, Alexander Selkirk lamented the loss of his lovely island which, from a distance and in company, seemed so much less of a horrible place.

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Treatment of acute lymphoid leukemia in children: Current regimens and future prospects

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Leukemia is the cause of death of more children than any other disease between the ages of 1 and 15 years. It accounts for 35% of all childhood cancer mortality. The incidence of leukemia in children under 16 years of age in the United States is 3.5/100,000/year.[1,2] Acute lymphoid leukemia (ALL) comprises 75 to 80% of all cases of leukemia in this age group. The incidence of the disease peaks between 3 and 5 years of age.[3] A slight male predominance is noted in most studies.[4]

The causes of acute lymphoid leukemia remain unknown. However, a number of possible predisposing factors have been investigated. Children with a variety of underlying conditions characterized by chromosomal abnormalities have been found to be at increased risk for developing leukemia. These include children with Down's syndrome,[5] Fanconi's anemia,[6] and Bloom's syndrome.[5] The concordance rate of ALL in identical twins is approximately 20%[7] and is particularly high in early childhood. Siblings of children with leukemia have a four-fold higher likelihood of developing the disease than the population at large.[5] Nevertheless, specific hereditary patterns have not been identified.

Both congenital and acquired immunodeficiency states may predispose to the development of lymphoid malignancies. Patients with the Wiskott-Aldrich syndrome, ataxia-telangiectasia, and hypogammaglobulinemia have been noted to be at increased risk,[8] as are children treated with immunosuppressive drugs.[9] It is presumed that failure of the normal "tumor surveillance" mechanisms may be responsible for this increased incidence of leukemia.

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Environmental toxins also have leukemogenic potential. Radiation exposure in utero, particularly when it occurs early in pregnancy, appears to be associated with an increased risk of childhood leukemia.[10] A number of chemical agents, including some categories of anticancer drugs, are potentially carcinogenic and have been implicated in the induction of leukemia. Studies concerning the incidence of leukemia and other malignancies in communities in close proximity to toxic waste dump sites are, as yet, inconclusive.

There is increasing evidence that viruses may be causative agents in at least some forms of leukemia. Thus, it is well known that certain retroviruses, which are large RNA viruses, may cause leukemia and lymphoma in a number of animal species, including cats, cattle, and simians.[11] Recently, a newly discovered retrovirus, called human T cell leukemia virus (HTLV), has been demonstrated in cultured T cells from a high proportion of Japanese and West Indian patients with T cell leukemia or lymphoma although it has been found in only a small number of T cell leukemia patients in the United States.[11] An HTLV-like virus has recently been isolated from patients with the acquired immunodeficiency syndrome (AIDS).[12]

The Epstein-Barr virus (EBV) has been detected in cultured cells of African children with Burkitt's lymphoma.[13] Cytogenetic studies of Burkitt's lymphoma cells frequently demonstrate a translocation from chromosome 8 to 14 (tr8;14). C-*myc*, which is the normal cellular homologue of a transforming gene from a retrovirus of avian leukemia, participates in the reciprocal translocation from chromosome 8, its normal location, to chromosome 14, at the region of fine immunoglobulin heavy chain synthesis.[14] This results in an increased expression of the C-*myc*

gene,[15] and μ heavy chains are found on the tumor cell surface.[16]

Although there is as yet no direct evidence of viral causation for the great majority of human malignancies, we are just beginning to elucidate the role of oncogenes in human carcinogenesis.

Clinical Presentation of ALL

At diagnosis, the bone marrow of children with ALL is usually packed with malignant lymphoblasts. There is a resultant failure of normal hematopoiesis. Most patients therefore present with signs and symptoms of bone marrow failure (Table I).[17] Usually the symptoms have been present for only a short period of time, although occasionally vague complaints may have been present for several months.

Fever, the most common symptom, is present in about 60% of children at the time of diagnosis. Fever may be secondary to the leukemic process itself, or may represent infection due to neutropenia. Pallor and fatigue result from anemia, which is present in the majority of patients. Petechiae, bruising, and mucous membrane bleeding occur in children who present with profound thrombocytopenia.

Leukemic infiltration of the liver, spleen, and lymph nodes produces hepatosplenomegaly and lymphadenopathy in a significant proportion of patients. Bone and joint pain may predominate in some children and is presumably the result of leukemic infiltration of the bony cortex and joint spaces.

Because of the protean nature of this disease, diagnosis is often delayed, with many children receiving treatment for a variety of nonspecific infections and other conditions (such as iron deficiency, idiopathic thrombocytopenic purpura, or juvenile rheumatoid arthritis) before the correct diagnosis is established. The possibility of leukemia should be kept in mind whenever a child presents with any of the above symptoms that cannot otherwise be explained. In questionable cases, a bone marrow examination should be performed prior to starting any treatment, such as steroid therapy, that might mask the diagnosis.

Supportive Measures

The prognosis for children with acute lymphoid leukemia has improved dramatically over the last two decades (Fig 1).[18] In 1948, the average life expectancy for a child with ALL was only three to four months. By 1961, the life expectancy had increased to almost 13 months, but nearly all patients still succumbed to the disease.[19] At least 50% of children with ALL now achieve long-term survival and probable cure.[20] The improved outlook resulted primarily from the development of effective chemotherapy programs, as well as improvements in supportive care.

TABLE I. Frequency of the More Common Presenting Complaints Among Children with ALL*

Clinical finding	Percent
Fever	61
Pallor	55
Hemorrhage	52
Anorexia	33
Fatigue	30
Bone pain	23
Abdominal pain	19
Joint pain	15
Lymphadenopathy	15
Weight loss	13

* From studies by the Southwest Oncology Group. Adapted from Fernbach,[17] with permission.

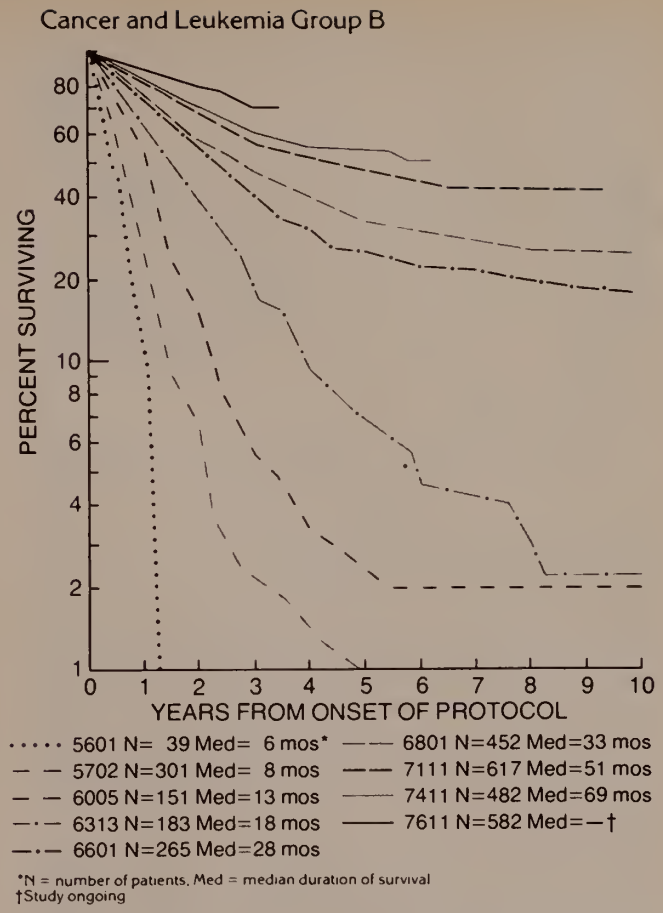

FIGURE 1. Survival of children with acute lymphoid leukemia on successive CALGB treatment protocols, 1956–1976 (from Freeman,[18] with permission).

Life-threatening metabolic derangements may be present at diagnosis, or may develop during the first few days of therapy when rapid tumor lysis occurs. Vigorous hydration, alkalinization of the urine, and the use of allopurinol will usually prevent the development of severe hyperuricemia with resultant uric acid nephropathy leading to renal shutdown. Children presenting with a large tumor cell burden, such as those with very high white blood counts or massive organomegaly, are at particular risk for metabolic complications. Rarely, extraordinary measures, including renal dialysis, are required to correct the initial metabolic derangements.

The development of newer, broad spectrum antimicrobial agents and their judicious use in neutropenic patients who have documented or suspected infection have dramatically reduced the number of deaths from bacterial sepsis that may occur before the patient achieves remission. The use of appropriate antibiotic therapy is equally critical during periods of neutropenia that follow aggressive antileukemic therapy. Certain viruses, including vari-

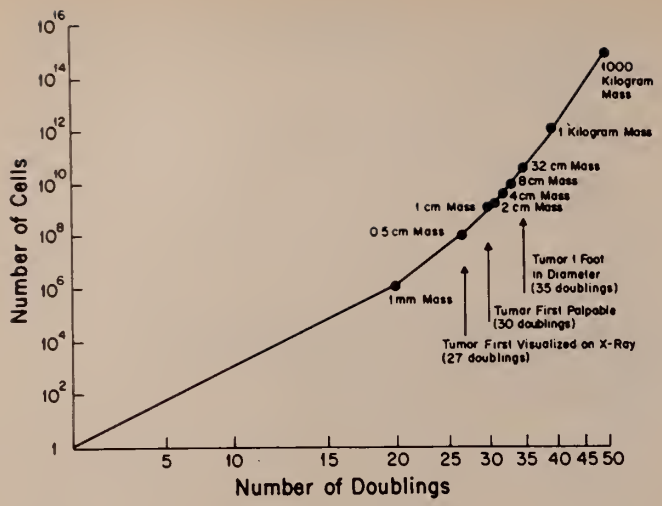

FIGURE 2. Theoretical growth rate during the process of tumor cell doubling (from Silver et al,[24] with permission).

cella-zoster virus and cytomegalovirus (CMV), may also cause life-threatening infections in immunocompromised hosts. Unfortunately, effective antiviral agents have not yet been developed, but the advent of a safe, live virus varicella vaccine[21] and the development of new techniques to screen blood products for CMV[22] should enable us to prevent these infections in most leukemic children in the near future.

Likewise the availability of blood component therapy, including packed red blood cells, leukocytes, and especially platelet concentrates, has contributed greatly to the care of these children during periods of disease-related bone marrow failure and iatrogenic bone marrow suppression.

Chemotherapy

The progress that has been made in the treatment of childhood leukemia has largely resulted from the development of increasingly effective programs of combination chemotherapy. These programs, in turn, have evolved from both theoretical considerations and empirical trials.

General concepts of chemotherapy. In theory, cancer begins when a single normal cell undergoes a malignant transformation. Subsequent tumor growth follows the mathematical model of Gompertz,[23] according to which tumor growth is at every instant exponential, but the growth constant is decreasing exponentially. By the time a malignant growth has become clinically detectable, the cells have undergone approximately 30 doublings (Fig 2).[24] Therefore, although a diagnosis of cancer may be made at an early clinical stage, essentially all tumors are recognized relatively late in their biological growth cycle. Since the likelihood of spontaneous mutation increases with increasing tumor cell burden,[25] clones resistant to the action of any single chemotherapeutic agent are likely to be present at the time of diagnosis. At late stages, the occurrence of relatively few doublings have a dramatic impact on total tumor burden.

The ability of chemotherapeutic drugs to kill tumor cells follows first-order kinetics; a constant percentage, rather than a constant number of cells, is killed by a given therapeutic maneuver. This behavior profoundly influences the therapeutic effect of cancer chemotherapy. For example, at diagnosis a child with ALL harbors approximately 10^{12} leukemic cells. A drug capable of killing 99.99% of these cells would reduce this burden to 10^8 cells, resulting in a complete clinical remission of the disease. The remaining 10^8 cells could obviously regrow, thereby causing a relapse. Cure most likely requires the total eradication of leukemic cells since in experimental models, a single cancer cell injected into a susceptible host can kill that animal.[26,27] Therefore, many drugs, with differing mechanisms of action, must be employed to prevent the emergence of resistant clones.

Resistance to a chemotherapeutic drug may also be induced when tumor cells are exposed to low concentrations of the drug for prolonged periods of time.[28] Therefore, intermittent, high-dose chemotherapy is likely to be more effective. If a number of effective chemotherapeutic drugs are available, alternating cycles of different agents that are non-cross resistant helps to prevent the emergence of resistant cell lines.[29]

Knowledge of cell cycle kinetics is important for appreciation of the cycle-specific action of most chemotherapeutic agents, and plays a role in the design of treatment protocols. In any tumor cell population, some cells are cycling continuously, while others may be in the G_0 or resting stage. With increasing tumor burden, there is a progressively larger proportion of the viable cell population entering a nonproliferative state.[30] Some chemotherapeutic drugs are capable of killing tumor cells in any stage of the cell cycle; others can kill only those cells that are actively proliferating. Some drugs are phase-specific, exerting their effect only during a single phase of the cell cycle. When phase-specific drugs such as antimetabolites are used, the duration of exposure of the tumor cells is as important as the peak drug levels achieved. Maintaining prolonged therapeutic levels results in maximum cell kill as tumor cells cycle through the particular phase affected by the drugs.

The great improvement in the prognosis of children with acute lymphoid leukemia that has occurred over the last two decades is due primarily to the development of treatment regimens employing various combinations of effective chemotherapeutic agents, and to the employment of CNS prophylaxis.

Induction phase. During the initial phase of treatment, a child presenting with florid leukemia is induced into a complete remission, in which there is no longer clinically detectable disease. This treatment restores normal hematopoiesis and decreases the risk of infection (due to neutropenia) and hemorrhage (due to thrombocytopenia). During this phase of therapy, the leukemic cell burden declines from approximately 10^{12} cells to less than 10^9 cells.

Two-drug induction regimens, utilizing weekly doses of vincristine and daily prednisone, produce a complete remission rate of more than 85% in childhood ALL.[31] When these two drugs are employed, the median time to remission is slightly less than four weeks. Ortega and associates[32] achieved an overall induction rate of 93%, utilizing the combination of prednisone, vincristine, and L-asparaginase. These three agents now constitute standard induction therapy in most current ALL protocols.

Some studies have suggested that the addition of an anthracycline antibiotic, either daunorubicin or adriamycin, as a fourth agent further improves the induction rate or remission duration.[33] However, the Cancer and Acute Leukemia Group B (CALGB), a national cooperative cancer study group, conducted two national trials testing the use of daunorubicin during both induction and maintenance therapy and was unable to show improvement in either induction rate or duration of complete remission (personal communication, E. D. Burgert and L. F. Sinks, 1985). Since the anthracycline antibiotics have potential cardiac toxicity, their routine use in the treatment of childhood ALL remains controversial.

Children who require more than four to six weeks of therapy to achieve complete remission, and those who fail to enter remission without the use of additional chemotherapeutic agents, are at great risk of suffering an early relapse of their disease.[34] Such patients require aggressive treatment regimens to prevent leukemic relapse.

Sanctuary phase. In the 1960s, as children with acute lymphoid leukemia began to achieve prolonged survival, the incidence of central nervous system relapse increased substantially. In its classic pattern, a child whose bone marrow remains in complete remission presents with signs and symptoms of increased intracranial pressure, and lumbar puncture reveals the presence of lymphoblasts in the CSF. Skipper[29] demonstrated that L1210 leukemia in mice "seeded" the CNS when the leukemic burden rose from 10^7 to 10^8 cells. A similar phenomenon occurs in children with ALL. When employed at standard doses, most of our currently used antileukemic drugs do not cross the blood-brain barrier in sufficient quantities to achieve therapeutic levels in the CSF. Leukemic cells, which are often present in the CNS in a subclinical or inapparent form at the time of diagnosis, may thus exist in a pharmacologic sanctuary. Eventually they may multiply to cause overt CNS leukemia. Although only about 2% of children with ALL have demonstrable disease in the CNS at diagnosis, children who do not receive specific therapy directed to the nervous system have a CNS relapse rate in excess of 50%.[35] In many cases, the development of meningeal leukemia is a harbinger of a systemic relapse, and thus augers a poor outcome.

In 1968, investigators at the St Jude Children's Research Hospital began employing 2,400 rad of cranial radiation therapy (CRT) in combination with intrathecal (IT) methotrexate early in the course of treatment. This treatment reduced the incidence of CNS leukemia to less than 10%.[36] At the same time, investigators in the CALGB using intrathecal methotrexate alone as CNS prophylaxis also demonstrated a reduction in the CNS relapse rate.[37]

In the 1970s, the Southwest Oncology Group (SWOG) conducted several randomized national trials. These trials compared the efficacy of repetitive doses of triple intrathecal chemotherapy (consisting of methotrexate, cytosine arabinoside (Ara-C), and hydrocortisone) without CRT with regimens that included 2,400 rad of CRT to prevent CNS leukemia. No difference was found in the incidence of CNS relapse or in the complete remission rate.[38,39] In another randomized trial, the Children's Cancer Study Group (CCSG) reduced the dose of CRT to 1,800 rad in an attempt to decrease the toxicity that results from irradiation of the CNS; this study showed no difference in the CNS relapse rates utilizing the two dose levels of radiotherapy.[40]

Some systemically administered chemotherapeutic agents are capable of penetrating the blood-brain barrier and achieving therapeutic concentrations in the CNS if they are given in sufficiently high doses. Such an approach has the added attraction of achieving drug penetration into other sanctuary sites, including the testis, ovary, and eye, where isolated relapses are also known to occur. In addition, the administration of high doses of effective agents should increase the overall leukemic cell kill, and thus have the potential of providing effective systemic consolidation therapy. Both methotrexate and Ara-C have been utilized in this fashion in conjunction with intrathecal therapy, and are being studied in a number of ongoing national trials. In a randomized study conducted by the CALGB evaluating the potential benefits of intermediate dose methotrexate (IDM), no significant protection against CNS relapse was demonstrated. However, the incidence of testicular leukemia was significantly lower in the cohort of patients who received intermediate dose methotrexate.[41] The CCSG investigated the use of radiation therapy given to multiple sanctuary sites; delivering 2,400 rad to the craniospinal axis and 1,200 rad given as extended field irradiation to the liver, spleen, kidneys, lower abdomen, and gonads. No survival advantage was demonstrated, and toxicity was excessive. This approach was later abandoned.[42]

The use of effective CNS prophylaxis has markedly reduced the incidence of meningeal leukemic relapse and thereby significantly improved the survival rate in childhood ALL. The optimum method of CNS prophylaxis re-

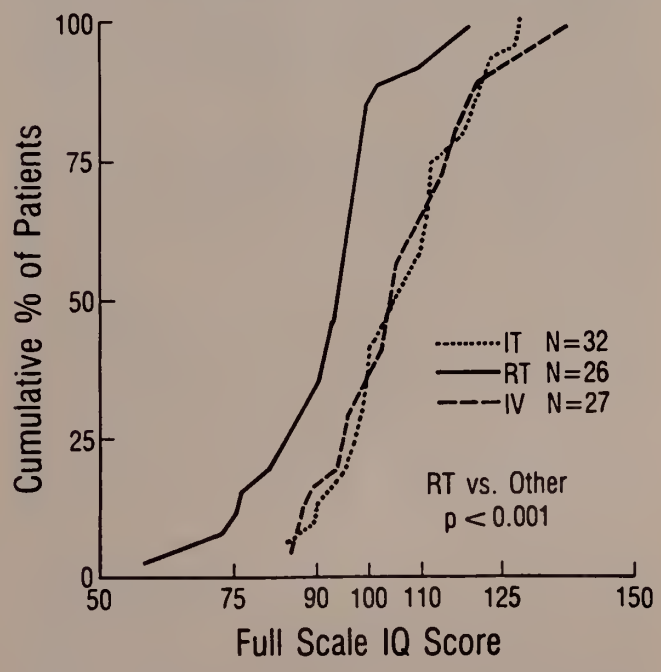

FIGURE 3. Distribution of IQ scores in patients treated by three methods of CNS prophylaxis. IT = intrathecal methotrexate only; RT = intrathecal methotrexate plus cranial irradiation; IV = intrathecal methotrexate plus intravenous intermediate dose methotrexate. (From Rowland et al,[43] with permission).

mains a point of controversy. There is growing concern about the late sequelae of CNS irradiation, particularly its effects on intellectual function (Fig 3).[43] Thus, there is a trend away from the use of cranial radiotherapy except in patients considered to be at particularly high risk for CNS relapse.

Maintenance phase. The concept of delivering maintenance therapy (also called continuation therapy) developed in the early 1960s. At that time it was realized that patients who entered remission still had subclinical disease that, if left untreated, resulted in subsequent relapse of their leukemia. Children with acute lymphoid leukemia who were randomized to receive maintenance treatment with 6-mercaptopurine (6-MP) following induction had a longer duration of remission than did those who received no postinduction therapy.[44] In 1968, the CALGB compared a regimen of 6-MP and methotrexate as maintenance therapy with the use of methotrexate alone. The two-drug maintenance regimen proved to be superior.[37] Subsequently, a number of other drug combinations have been studied. In one study the use of methotrexate alone, methotrexate plus 6-MP, methotrexate plus 6-MP plus cyclophosphamide, and methotrexate plus 6-MP plus cyclophosphamide plus Ara-C were compared. The two-drug combination (methotrexate plus 6-MP) resulted in the longest remission duration and produced the least toxicity.[45] The combination of daily 6-MP and weekly methotrexate remains the backbone of most maintenance regimens for treating ALL in use today.

Studies evaluating the efficacy of adding periodic pulses of vincristine and prednisone during maintenance treatment have produced conflicting results. Studies by both the CALGB and the Pediatric Oncology Group (POG) have demonstrated benefit from the use of such reinduction pulse therapy,[46,47] but the CCSG has found no improvement resulting from the addition of vincristine and prednisone pulses to maintenance therapy of 6-MP plus methotrexate.[34]

There is no agreement as to how long to continue treatment for patients who remain continuously free of disease. In the early 1970s, the CALGB randomized patients to receive either five or seven years of maintenance therapy, and found no difference between the two.[48] The CCSG subsequently compared three versus five years of maintenance. There was no statistically significant difference in relapse-free survival, although there was a suggestion that males received some benefit from the additional two years of therapy.[49,50] The majority of relapses in this disease occur within three years of diagnosis, and most studies currently deliver maintenance therapy for two and one half to three years, although the optimum duration of treatment has not yet been determined.

If one accepts the concept that intermittent high-dose chemotherapy, preferably with alternating cycles of non-cross resistant drugs, is the best way to prevent the emergence of resistant cell lines, then the use of low-dose, long-term maintenance therapy may not be the most rational approach to treatment. A number of protocols are now investigating the use of intensive consolidation courses —delivered shortly after remission is achieved—in an effort to obtain maximum leukemic cell kill early in therapy. A study in West Germany by the Berlin-Munster-Frankfort (BMF) group reported excellent results utilizing a very intensive consolidation phase.[51] Relatively short but intensive treatment programs have already proven to be as effective as longer regimens in the treatment of acute myeloid leukemia (AML). Similar approaches will probably be tested in at least some subcategories of childhood ALL in the near future.

High-dose systemic chemotherapy often penetrates sanctuary sites as well, providing protection against extramedullary relapse. Consolidation therapy, therefore, overlaps with the sanctuary phase of treatment.

Prognostic Factors

At least one half of the children with ALL may now be expected to survive their disease by the utilization of current therapeutic regimens.[20] Unfortunately, this means that more than 40% of affected children still succumb to leukemia. Most relapses occur within two to three years of diagnosis, but 15 to 25% of children in whom therapy is discontinued after three years of continuous remission will subsequently relapse, usually within one to two years of cessation of therapy.[52] Although the causes of treatment failure in an individual patient are often not clear, a number of prognostic variables have now been identified. These variables include initial white blood cell count, age, immunophenotype, sex, race, the presence of hepatosplenomegaly or lymphadenopathy, chromosomal findings, lymphoblast morphology, the presence of CNS disease, initial hemoglobin, and presenting platelet count.[53,54] However, not all studies confirm all of these factors as having prognostic significance.

White blood cell count. The single most important predictor of outcome in childhood ALL is the white blood cell (WBC) count at presentation.[55] The higher the initial WBC count, the more likely the child is to suffer a relapse (Fig 4).[41] This is presumably because patients with a high WBC count have a very large tumor cell burden and are consequently likely to have resistant clones present. Other evidence of bulky disease, including massive organomegaly and lymphadenopathy, also appears to place patients at an increased risk of relapse, although specific correlation with prognosis has been more difficult to quantify.[53]

Age. Children between 2 and 10 years of age have a better prognosis than do children less than 2 or greater than 10 years of age.[42,55] Infants less than one year of age have a particularly poor prognosis.[56] Teenagers over age 15 years likewise have a poor outlook,[55] and adults fare even less well.[57] It is not clear if the influence of age on prognosis is a result of differing host factors, or if different disease processes are represented. It is known, for instance, that adolescents have a higher incidence of the T cell type of ALL[58] and that the majority of children less than one year of age have lymphoblasts that do not express the common ALL (CALL) antigen.[59]

Immunophenotype. Acute lymphoid leukemia is now known to represent a heterogeneous group of lymphoid malignancies composed of a variety of immunologic subtypes. In 80 to 85% of patients with ALL, the lymphoblasts express neither T cell antigens nor the surface immunoglobulins characteristic of B lymphocytes, and thus have been termed "null cells." Between 15 and 20% of children with ALL have that type which is clearly derived

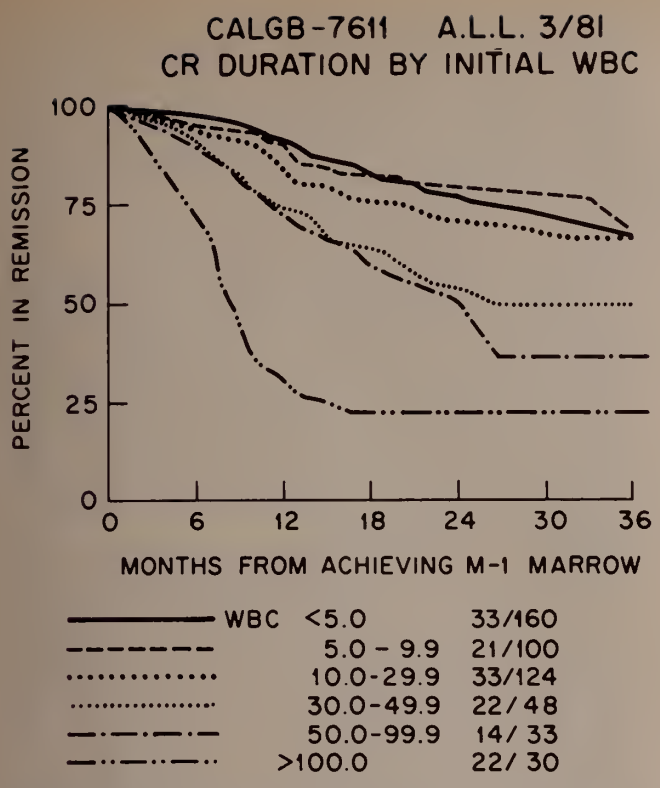

FIGURE 4. Duration of remission as affected by initial white blood cell count in patients on CALGB protocol 7611 (from Freeman et al,[41] with permission).

from the T cell line. This is seen more commonly in adolescents, and a significant male predominance has been noted. Less than 1% of children have B cell ALL, which often, but not always, represents a leukemic transformation of Burkitt's lymphoma. More recently, in approximately 20% of patients with so-called null cell ALL, the lymphoblasts have been found to contain cytoplasmic IgM, and such patients are now considered to have "pre-B cell" leukemia.[60] With the development of monoclonal antibodies, the immunologic separation of ALL into specific phenotypes has been greatly refined. It is now believed that essentially all cases of ALL, with the exception of the subsets that clearly demonstrate T cell antigens, are of B cell lineage, arising at various stages of differentiation.

There is much controversy in the literature concerning the role of immunophenotype as an independent prognostic variable (Fig 5).[61] There is wide agreement that children with the true B cell type of ALL have a dismal outlook. Recent studies indicate that both the induction rate and the remission duration of children with T cell ALL are worse than for children with null cell ALL.[59] Patients with T cell disease and an initial WBC greater than 50,000/μL have a particularly poor outlook. However, other researchers have reported that the T cell immunophenotype may not be an independent prognostic factor.[62] In another study, children with pre-B cell leukemia had a shorter median duration of remission and a higher incidence of CNS relapse than did children with null cell ALL.[63]

Greaves and colleagues[64] reported that children with acute lymphoid leukemia whose lymphoblasts are negative for the CALL antigen have a significantly shorter duration of remission than do the remainder of children with null cell ALL. In contrast, recent studies by the POG in which approximately 10% of the cases of null cell ALL were CALL antigen negative have shown no difference in prognosis between CALL antigen positive and CALL antigen negative patients.[61]

Studies conducted in West Germany by the BMF group failed to show any prognostic significance for cell surface markers, but this may simply indicate that when extremely aggressive therapy is used for all patients, certain prognostic variables may be overridden.[51] Clearly, the immunological separation of ALL into several phenotypes represents a major advance in understanding the disease and may help tailor treatment to the needs of specific subgroups of patients. However, there is as yet no universal agreement about its prognostic or therapeutic implications.

Cytogenetics. There is a growing body of evidence that cytogenetic abnormalities have major prognostic significance in leukemia. In approximately 60% of patients with ALL, chromosomal analysis reveals an abnormal karyotype.[65] The presence of hypodiploidy or pseudodiploidy appears to impart a relatively poor prognosis.[65,66] In contrast, children with null cell ALL in which chromosomal findings are normal or those that demonstrate hyperdiploidy tend to have a favorable prognosis.[65] Approximately 5% of children with ALL have lymphoblasts containing the Philadelphia (Ph^1) chromosome.[67] Some of these cases may represent a lymphoid blast crisis of chronic myeloid leukemia (CML). However, most cases are likely to be de novo ALL, since the Ph^1 chromosome often disappears during periods of remission, a phenomenon that would be highly unusual in CML. The presence of the Ph^1 chromosome in children with ALL imparts a poor prognosis. Certain other translocations, such as tr(8;14) (characteristic of Burkitt's lymphoma), and tr(4;11) also indicate an unfavorable prognosis.[68,69]

Morphology. Acute lymphoid leukemia is subdivided into three morphologic groups (L_1, L_2, and L_3) by the French, American, and British (FAB) classification (Table II).[70] The lymphoblasts of more than 80% of cases of childhood ALL show the L_1 morphology. L_3 morphology

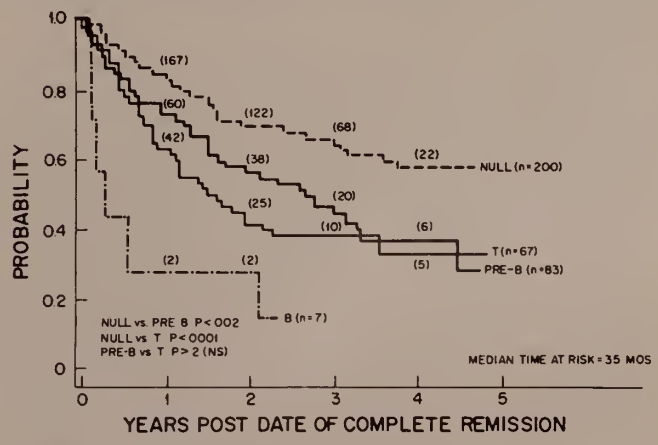

FIGURE 5. Duration of complete remission as affected by immunophenotype (from Pullen et al,[61] with permission). The curves show duration of continuous complete remission (CCR) for the null, pre-B, and T cell groups of patients with acute lymphoid leukemia.

TABLE II. FAB Morphologic Classification of Lymphoblasts in ALL*

Cytological features	L_1	L_2	L_3
Cell size	Small cells predominate	Large, heterogeneous in size	Large and homogeneous
Nuclear chromatin	Homogeneous in any one case	Variable; heterogeneous in any one case	Finely stippled and homogeneous
Nuclear shape	Regular, occasional clefting or indentation	Irregular, clefting and indentation common	Regular; oval to round
Nucleoli	Not visible or small and inconspicuous	One or more present; often large	Prominent; one or more vesicular
Amount of cytoplasm	Scanty	Variable; often moderately abundant	Moderately abundant
Basophilia of cytoplasm	Slight or moderate; rarely intense	Variable; deep in some	Very deep
Cytoplasmic vacuolation	Variable	Variable	Often prominent

* From Bennett et al,[70] with permission.

is classically seen in patients with Burkitt's lymphoma involving the bone marrow, which carries a very poor prognosis. It has been suggested that L_1 lymphoblast morphology is more favorable than L_2 morphology, but the POG was unable to confirm the usefulness of FAB classification as an independent prognostic variable.[71]

Sex. Girls with acute lymphoid leukemia tend to fare somewhat better than do boys. This is accounted for in part by the higher relapse rate in boys following the cessation of therapy.[72]

Race. Although the incidence of leukemia is slightly lower in black children, the prognosis is worse.[73] Black children have a higher incidence of pre-B cell ALL and T cell ALL.[74]

There is obviously conflicting data concerning the prognostic value of many of the variables studied, with the exception of age and WBC count at presentation. It should be kept in mind that variability in results among studies may be due to treatment differences. In addition, multifactorial analysis is necessary before independent significance may be attributed to a specific variable, since there is a great deal of overlap of prognostic features. For instance, analysis of 90 infants less than 18 months of age by the POG indicated that these patients were more likely than patients in the study group as a whole to have a high WBC count, massive organomegaly, and CNS disease at the time of presentation.[56] Similarly, adolescents were found to have a higher incidence of T cell ALL, be more often male than female, have a higher WBC count, and have a higher percentage of patients whose leukemia cells demonstrate hypodiploidy or pseudodiploidy on cytogenetic analysis.[58]

Despite these difficulties, the elucidation of prognostic factors in ALL should allow for the utilization of different treatment protocols in different subgroups of patients, with the purpose of increasing the survival rate for children at high risk of relapse while avoiding unnecessary toxicity in children whose outlook is more favorable.

Treatment of Relapse

Despite the dramatic improvement in survival rates attained over the last two decades, almost one half of children with ALL still experience recurrence either in the bone marrow or in one or more extramedullary sites. At least 25% of the children who experience an isolated CNS relapse may probably be salvaged by utilizing aggressive intrathecal chemotherapy and CNS irradiation.[75-77] Systemic intensification therapy, preferably utilizing some new agents, is usually necessary to prevent subsequent relapse in the bone marrow.

Patients who suffer an isolated testicular relapse while on therapy have a relatively poor prognosis.[78] Such patients are at high risk of early bone marrow relapse, presumably because they have occult residual disease beyond the testes.[79] These patients should be treated with both testicular irradiation and systemic chemotherapy regimens containing drugs that are not cross-resistant with those drugs previously employed. Isolated testicular relapse that occurs following the elective cessation of therapy carries a much more favorable prognosis.[78] Most patients may be salvaged by utilizing a combination of testicular irradiation and systemic chemotherapy.

The occurrence of a hematologic relapse during chemotherapy generally represents the repopulation of the bone marrow with resistant leukemic cells and augers a poor outcome. Although most patients may be reinduced into remission, second and subsequent remissions tend to be of short duration, and almost all such patients eventually die of leukemia if they are treated with conventional therapy.[80] Only those patients who undergo allogeneic bone marrow transplantation following attainment of second remission have a realistic chance for cure.[81] Long term disease-free survival rates in the range of 30% have been reported in this group of children. Patients who experience a bone marrow relapse more than one year following the cessation of therapy tend to be less resistant to conventional maintenance agents, and a small percentage of such patients may be salvaged by using further chemotherapy.[82]

Projections for the Future

Cure rates in the range of 50 to 60% reflect the tremendous progress that has been made in the treatment of childhood ALL over the last two decades. However, therapy that fails to prevent almost one half of the patients from dying of disease is surely in need of major improvement. Ongoing research involving new chemotherapeutic agents and new drug combinations aims at preventing the emergence of drug resistance, which is the major cause of treatment failure. More effective salvage therapy is clearly needed for those patients who do experience leukemic relapse. More targeted therapy is necessary if cure rates are to be maximized, while minimizing toxicities and late sequelae of therapy in the increasing number of children who are surviving this disease.

Current chemotherapeutic agents are nonspecific cell toxins, which affect normal as well as malignant cells and therefore cause considerable toxicity to normal body tissues. The development of hybridoma technology for the production of monoclonal antibodies has opened the possibility of directing chemotherapeutic agents to leukemic cells, thus increasing the concentration of the drugs in the cancer cells while simultaneously decreasing toxicity. Monoclonal antibodies have already demonstrated some activity in clinical studies when used as serotherapy.[83,84] They may be used as immunotoxins, by being bound to plant toxins such as ricin, and then acting as a "homing device" by delivering the toxin to the cancer cells.[85,86]

As previously noted, bone marrow transplantation usually offers the only chance for cure of children experiencing a bone marrow relapse while being treated for ALL. It may also be the treatment of choice for patients in first remission who are at very high risk of relapse. Unfortunately, only about one third of patients have a histocompatibility-leukocyte antigen (HLA) identical donor. Even when a matched donor is available, graft-versus-host disease (GVHD) may still be a major problem. The use of autologous bone marrow transplantation is an attractive alternative, since it would avoid these problems. However, even the bone marrow of a patient in remission likely contains small numbers of leukemic cells and reinfusion of these leukemic cells would clearly defeat the purpose of the procedure. Monoclonal antibodies are currently being investigated for their ability to purge bone marrow of residual leukemic cells. If successful, this technique would provide new possibilities of cure for children with relatively resistant disease.

The role of immunotherapy in the treatment of ALL remains unclear. Mathé and coworkers[87] reported improved results in children with ALL by using Bacillus of Calmette and Guerin (BCG) vaccine in addition to chemotherapy. However, other studies have not confirmed Mathé's results.[88] Pavlovsky and associates[89] reported that levamisole, an antihelminthic agent that appears to stimulate the immune system in the immunocompromised host, prolonged the duration of remission in standard-risk patients with ALL. There are no large, controlled studies that demonstrate a clear benefit from immunotherapy in the treatment of ALL. However, there is increased interest in a variety of immunostimulants and the interferon compounds, as well as the demonstrated ability of lymphokines to alter helper and suppressor T cells and natural killer cells. These modalities may be used as biological response modifiers in future clinical trials.

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ERRATUM

In the article entitled, "The child with short stature," by Drs Oberfield and Levine (*NY State J Med* 1986; 86:15–21), Figure 5 was erroneously cited from reference 66. In actuality this figure was reprinted from reference 65 (*N Engl J Med* 1985; 312:4–9), with permission.

Primary cardiac tumor in an 18-year-old man: Manifestations of a familial cancer syndrome

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Primary cardiac tumors are rare, being found in .0017 to .28% of patients in autopsy series.[1] Malignant tumors comprise only one fourth of this total.[2] Familial occurrence of myxomas has been reported,[3] as has the familial occurrence of malignant tumors.[4,5] The following report is of a case of primary cardiac sarcoma in an 18-year-old man whose sibling had died of rhabdomyosarcoma.

CASE REPORT

An 18-year-old man was admitted to the hospital with complaints of dyspnea and chest pain. A diagnosis of cardiac tamponade was made after a chest radiograph showed an enlarged cardiac silhouette and an echocardiogram confirmed pericardial effusion. A pericardial drainage tube was placed and 1,000 cc of bloody fluid was obtained with relief of symptoms. Fluid analysis revealed a protein content of 5.7 g/dL; a WBC count of 229/cc with 45% polys and 55% lymphocytes; and 59,000 red blood cells/cc. Atrial flutter was treated with digoxin and verapamil. Oral corticosteroid therapy was initiated for possible viral pericarditis. A repeat two-dimensional and M-mode echocardiographic examination suggested the presence of a mass; the patient was then transferred to our institution.

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Examination at our institution revealed a thin, white adolescent in no acute distress. Blood pressure was 106/80 mm Hg; the pulse was 80 and regular. No pulsus paradoxus was demonstrable. The jugular venous pulse was normal. Cardiac examination revealed normal first and second heart sounds. No murmur, rub, or tumor "plop" was noted. There was no evidence of phakomatoses. The remainder of the examination was unremarkable. Complete blood count, automated chemistry profile, and prothrombin time were normal except for a platelet count of 689,000/μL (normal, 150 to 350,000/μL), an alkaline phosphatase of 171 IU/L (normal, 30 to 115 IU/L), and a lactic dehydrogenase of 240 IU/L (normal, 60 to 200 IU/L). Chest radiograph revealed a mildly enlarged cardiac silhouette with clear lung fields. Electrocardiogram showed sinus rhythm with nonspecific ST and T wave changes.

The family history was notable because an older brother had died at 3 years of age of a metastatic embryonal rhabdomyosarcoma originating in the gluteal region that was diagnosed at age 2½. The patient's father had died in a plane accident. His mother, three grandparents, maternal aunt, paternal uncle, and 13-year-old brother were alive and well. His maternal grandmother had breast carcinoma that was diagnosed at age 38.

Repeat echocardiographic examination defined a mass in the region bounded by the superior vena cava, right atrial appendage, and aorta, as well as a small pericardial effusion, mitral valve prolapse, and a persistent left-sided superior vena cava (Fig 1). Subsequently, a computerized tomographic (CT) examination of the chest revealed pericardial thickening anterior to the pulmonary outflow tract and aorta, and extending into the pericardial space medial to the superior vena cava and posterior behind the ascending aorta. Following contrast injection, two filling defects were noted in the right atrial cavity

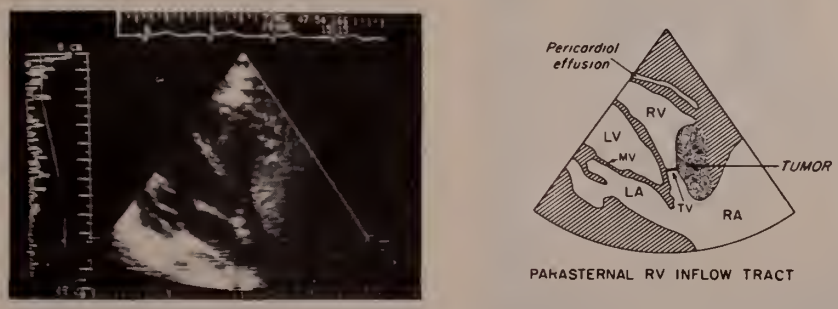

FIGURE 1. Two dimensional echocardiogram (left) and identifying line drawing (right), obtained with transducer in the fourth intercostal space, parasternal region, demonstrating the right ventricular inflow tract. A mass is seen adherent to the right atrial free wall. A small pericardial effusion is present. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; TV = tricuspid valve; VS = ventricular septum.

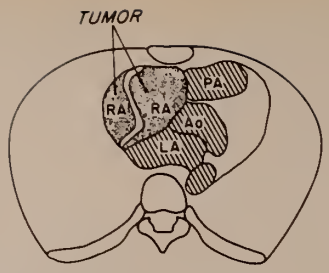

FIGURE 2. Computerized tomogram of the mediastinum at the level of the right atrium (left) and identifying line drawing (right). Contrast is present within the pulmonary artery (PA), left atrium (LA), and aorta (Ao). Tumor is outlined within the right atrium, the cavity of which is narrowed to a channel-like configuration.

suggesting the presence of a tumor or clot (Fig 2).

Cardiac catheterization was performed to further delineate the lesion. An intracavitary mass diffusely adherent to the right atrial wall was outlined. It narrowed the chamber to a channel-like configuration barely allowing passage of a 5-French catheter. The mass extended into the superior vena cava, but the right ventricle and pulmonary arteries appeared normal. Following contrast injection of the right coronary artery, a "blush" extending to the region of the right atrium was visualized. Right and left heart pressures were normal. No right atrial gradient was noted; however, right sided pressures were low, and a fluid filled catheter system was used in recording the pressures.

At the time of surgery, a tumor mass was noted at the junction of the superior vena cava and right atrium extending onto the anterior aorta. The mass also occupied the region between the aorta and the right ventricle, extending laterally to the main pulmonary artery, right pulmonary artery, and superior pulmonary vein. A biopsy of the mass in the region of the right atrium was performed. Histologic examination disclosed undifferentiated malignant spindle cells, potentially of connective tissue of vascular or mesothelial derivation. Pericardial biopsy showed fibrosis with granulation tissue and mesothelial reaction. The tumor was deemed unresectable and chemotherapy was subsequently initiated with doxorubicin.

Discussion

Primary malignant cardiac tumors are uncommon, occurring from 20 to 40 times less frequently than tumors metastatic to the heart.[1,6] They are slightly more frequent in men and usually occur during the third and fifth decades.[1] Of the 117 primary cardiac malignancies reported in one series,[2] 39 were angiosarcomas, 24 were rhabdomyosarcomas, 19 were mesotheliomas, and 13 were fibrosarcomas. The spindle cell sarcoma, present in this patient, represents a less differentiated cell line.

Cardiac involvement by tumor may produce intracavitary obstruction, distortion of valves, coronary artery obstruction, involvement of the conduction system, embolism (both pulmonary and systemic), and hemopericardium.[7] The clinical presentation may include dyspnea, chest pain, superior vena cava syndrome, cerebrovascular accident, pulmonary hypertension, pulmonary stenosis, rhythm disturbance, pericardial effusion with or without tamponade, myocardial rupture, or sudden death.[1,6,7] In descending order of frequency, the right atrium, left atrium, right ventricle, and left ventricle may be affected.[1]

Echocardiography has proved useful in diagnosing both right- and left-sided cardiac masses, most of which have been myxomas.[8] The findings are usually those of a cloud or mass occupying the space behind the atrioventricular valve, although other findings have been reported as well.

Previous reports have shown that CT scan may be useful in the diagnosis of pericardial disease and intracardiac masses.[9] Some have thought this method to be less useful for delineating cardiac masses due to potential problems with image resolution resulting from cardiac motion. Newer scanners with rapid scan-times and high resolution may overcome this potential drawback.[9] Our case illustrates that CT examination may be helpful in defining the location and extent of intra- or pericardiac masses.

The absence of signs of superior vena cava obstruction in this patient might be explained by presence of the left superior vena cava as noted on echocardiogram and well developed collaterals through the azygous system to the inferior vena cava.

Of additional interest in this case was the occurrence of sarcomas in siblings. Familial occurrence of cardiac myxomas has been well documented.[3] Sarcomas are known to occur with increased frequency in tuberous sclerosis, neurofibromatosis, and the basal cell nevus syndrome[5]; none of these syndromes were evident in the family reported here. A familial cancer syndrome including soft tissue sarcomas, breast, lung, brain and adrenal carcinomas, and leukemia has been described. Early age of presentation and multiple tumors in individuals have been noted. Autosomal dominance has also been postulated.[4,5]

This case may represent an expression of a familial cancer syndrome. The occurrence of sarcomas in two of three children is consistent with previous reports in which a young age of presentation of malignancy has been noted. While an autosomal dominant mode of inheritance appears to be implicated, environmental influences may play a role as well.[5] Close observation of this family appears warranted.

Acknowledgments. The authors thank Dr Leonard Bibberman for referring this patient, Ms Mary Cindrich for her technical assistance, and Ms Jeannette Frantz and Mrs Kay Thomas for their clerical assistance.

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See also pp 172-173.

Bifrontal primary central nervous system lymphoma

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Primary malignant lymphoma of the central nervous system (CNS) is a rare entity[1-6] accounting for only 0.04 to 2.0% of all malignant lymphomas[2,5] and 0.85 to 1.5% of all primary CNS tumors.[2,3] The incidence of primary malignant lymphoma of the CNS increases up to sixfold in patients with immunologic disorders[7] such as systemic lupus erythematosus,[8] Sjögren's syndrome,[9] rheumatoid arthritis,[10] immunoglobulin A deficiency,[11] and primary or acquired immunodeficiency.[12] A 350-fold increased risk has been reported in the organ transplant population[13] and recently an increased risk has been noted in those persons with the acquired immunodeficiency syndrome (AIDS).[14]

Primary CNS lymphomas have a tendency to be infiltrative and multicentric,[5,6,15] and may simulate primary or metastatic brain tumors. Only seven cases of bifrontal primary CNS lymphoma have been mentioned previously in the literature in the context of a series of case reports but without details of the clinical and pathologic findings.[1-6] We report an eighth case: primary CNS lymphoma occurring in a previously healthy woman.

CASE REPORT

A 70-year-old woman presented with a four-week history of frontal headaches. For two weeks prior to admission the family described personality changes associated with episodes of confusion during which the patient closed her eyes, tilted her head forward, and was seemingly out of contact with her environment. She could be aroused from this state but she had no recall as to what had happened immediately before and during these episodes.

On several occasions the patient had urinary incontinence in public places and had showed no concern. She was reported to repeat irrelevant phrases. She was a known hypertensive for seven years and was under good control with Midoril and diazepam; however, she failed to take her medication during the last two weeks.

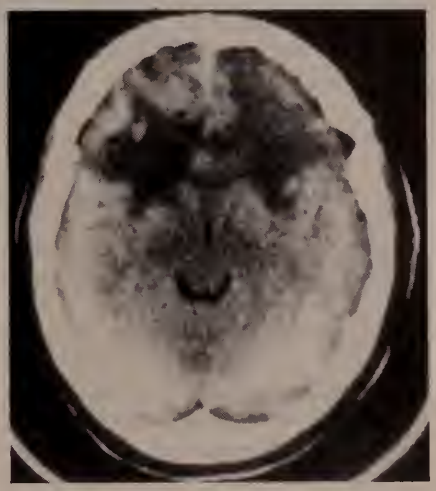

FIGURE 1. CT scan of brain without contrast showing large hypodense abnormality in butterfly distribution involving both frontal lobes.

On physical examination the patient was found to be obese with a blood pressure of 170/110 mm Hg and a regular pulse. There were no palpable abnormal masses or lymphadenopathy noted. The patient was disoriented as to time but oriented for place and person. During her hospitalization she had several episodes similar to those described by her family; within minutes she was relatively alert and fairly well oriented except for time. She was knowledgeable about current events and could identify objects and carry out commands promptly and correctly. She calculated and reversed without error. Her pupils were equal and constricted to light. Cranial and peripheral nerves were within normal limits except for an old central scotoma. All modalities of somatosensory perception were intact. By the third hospital day her episodes of disorientation and alteration of consciousness had become so frequent as to be present most of the time.

A computed tomographic (CT) scan without contrast revealed a huge hypodense abnormality in a butterfly distribution involving both frontal lobes (Fig 1). After contrast the CT scan revealed four hyperdense lesions, all within the described bifrontal hypodense area. There was a ring-enhancing lesion in the left frontal lobe, an oval shaped density in the anterior corpus callosum, and a round density with a smaller satellite lesion in the right frontal lobe (Fig 2). One of the interpretations of the CT scan was metastatic disease; however, search for a primary lesion was negative. Peripheral blood and spinal fluid studies were normal except for a CSF total protein of 94 mg%.

Twelve days after admission to the hospital a brain biopsy of the right frontal lobe lesion was performed. On the fifth postoperative day radiation therapy was begun to the whole brain, including additional boosts to the involved areas. Eighteen days after surgery, after receiving 1,300 rad of radiation, the patient had two convulsions. Following these she became diaphoretic, dyspneic, and unresponsive and expired.

On pathologic examination the surgical specimen consisted of several fragments of brain tissue and meninges measuring between 0.5 to 3.0 cm in largest diameter. On section there were areas of softening with a pale grey-tan color. On microscopic examination multifocal infiltrates of large lymphocytes with large nuclei, prominent nucleoli, scanty amphophilic cytoplasm, and frequent mitotic figures were seen (Fig 3), forming homogenous tumor masses that had a tendency to be located around vessels (Fig 4). There was considerable necrosis of the tumor. Immunoperoxidase staining showed a monoclonal lymphocytic population expressing intracytoplasmic IgM and kappa light chain (Fig 5). A diagnosis of large cell lymphoma, immunoblastic type (International Lymphoma Formulation), or histiocytic type (Rappaport's classification) was made.

At autopsy the brain weighed 1320 g. A surgical defect was located on the superior aspect of the right frontal lobe. In horizontal serial sections this defect measured 5.0 cm

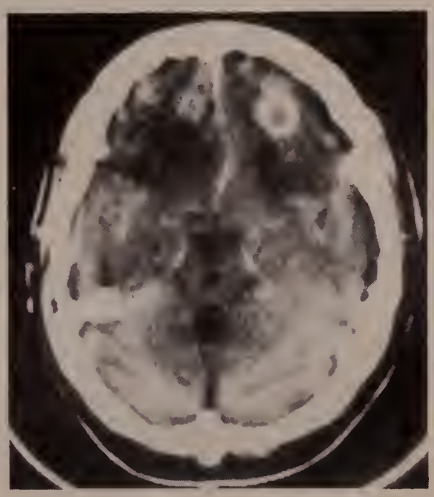

FIGURE 2. CT scan of brain after contrast showing hyperdense masses in frontal lobes with ring enhancing lesion in left frontal lobe.

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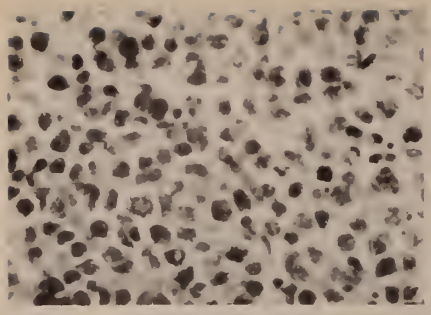

FIGURE 3. Brain biopsy. Tumor formed by large lymphocytes with scanty cytoplasm, prominent nuclei with reticulated chromatin, and presence of frequent mitoses. (Hematoxylin and eosin stain; original magnification X 1,200.)

in largest diameter and was surrounded by a slightly necrotic, yellow-hued centrum semiovale. In addition, two other well-circumscribed masses were present, one within the genu of the corpus callosum measuring 1.2 cm in greatest diameter, and the other in the left frontal lobe towards the orbital surface measuring 1.5 cm in greatest diameter. Both lesions had grey-white centers and tawny halos approximately 0.3 cm in thickness (Fig 6). Both frontal lobes were severely edematous and the junction between cortex and centrum semiovale was blurred. This edema stopped abruptly at the level of the anterior aspect of the insula. The remaining cerebral substance, as well as the cerebellum and brain stem, did not reveal any abnormalities. The ventricular system was slightly dilated. No viable tumor was identified microscopically. The necrotic tissue was surrounded by a rim of granulation tissue and there was considerable reactive gliosis in the edematous cerebral tissue. The remainder of the autopsy revealed massive pulmonary thromboemboli as a cause of death and failed to reveal any evidence of systemic lymphoma.

Discussion

The histogenesis of the tumor cell of a primary CNS lymphoma has aroused controversy in the past.[1-6] With the advent of immunologic cell markers, it has been demonstrated that the cell of origin is a transformed lymphocyte most often with monoclonal B cell characteristics.[16] The origin of the tumor cells from transformed B lymphocytes has also recently been demonstrated in cell cultures, by heterotransplantations, and tumor growth in brain and viscera in immunosuppressed newborn hamsters.[17] The majority of these tumors are composed of large cells with the characteristics of "histiocytic" lymphoma according to Rappaport's classification,[18] or immunoblastic sarcoma by Lukes and Collins' classification.[19] Histologically, the tumor characteristically grows concentrically around blood vessel walls suggesting an origin from these areas. The present case exhibited these morphologic features and the presence of intracytoplasmic IgM and kappa immunoglobulin.

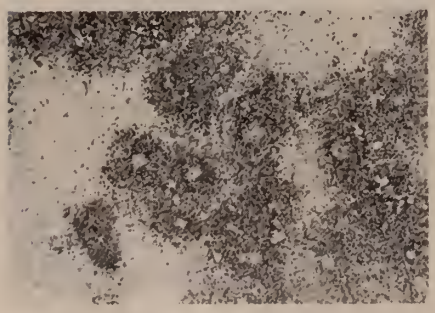

FIGURE 4. Multiple tumor infiltrates around vessels. (Hematoxylin and eosin stain; original magnification X 112.)

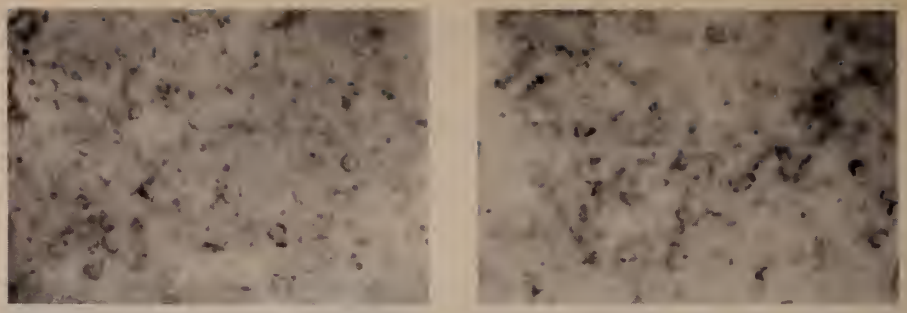

FIGURE 5. Immunoperoxidase stain for IgM heavy chain (left); immunoperoxidase stain for kappa light chain (right).

Primary CNS lymphomas tend to be multicentric (46% of cases) involving extensive areas that cannot always be seen grossly but are demonstrated by CT scan.[5,6,20] The tumor may be supra- or infra-tentorial in location. The most common sites of involvement, in order of frequency, are cerebral hemispheres, particularly the frontal lobes; deep cerebral nuclei; periventricular areas; and the cerebellum. In solitary lesions, it appears that the frontal lobes are the most frequently involved, but bilateral frontal involvement, as in the case described here, is a rare occurrence with only seven cases previously reported (Table).[1-6]

Central nervous system lymphoma is clinically characterized by varied, nonspecific neurologic symptoms related primarily to elevated intracranial pressure and focal neurologic deficit suggesting an expansive intracranial growth. These patients usually have a rapid, fulminant course and short life expectancy.[4,6,21] The clinical and laboratory investigations including radiographic studies are usually not helpful in establishing the correct diagnosis before surgery. Single lesions of primary CNS lymphoma may be clinically confused with glioblastoma multiforme, brain infarct, and brain abscess. Multifocal lesions also mimic metastatic tumor.

On CT scan, CNS lymphomas may be seen as a hypodense, isodense, or hyperdense tumor with intense postcontrast enhancement and a peripheral zone of edema.[5,13,20] If no hypodense areas are identified, an absence of necro-

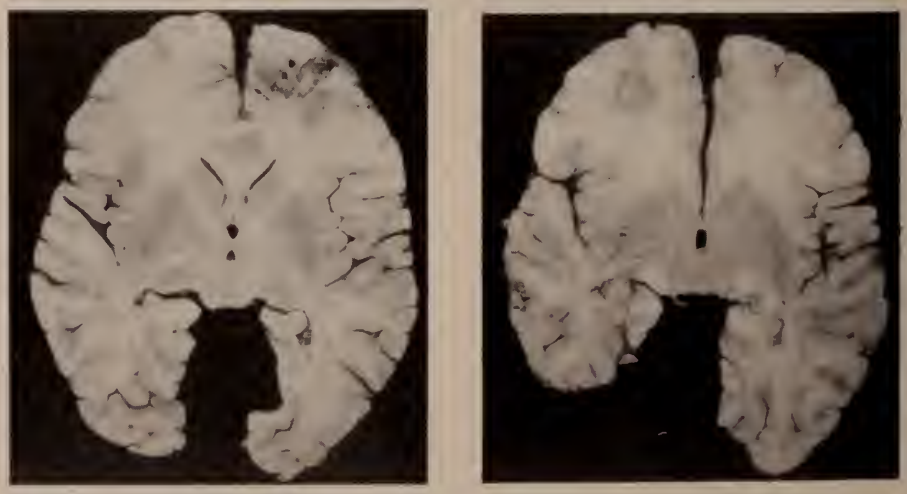

FIGURE 6. Horizontal sections of the brain showing a well-circumscribed mass in genu of corpus callosum and surgical defect in the right frontal lobe (left) and a well-circumscribed lesion in the left frontal lobe (right).

TABLE. Bifrontal Primary Central Nervous System Lymphoma: Review of the Literature

Author/Year	Age/Sex	Clinical presentation	Radiographic studies	Treatment	Follow-up/Pathology
Schaumburg/1972	50/F	Stupor; coma	Angiography	None	Died after 6 mo/diffuse bifrontal
Littman/1975	49F	Hemiparesia dysphasia	—	WBR* (4,600 rad)	Alive after 3 mo/bifrontal, left parietal
Shankar/1978	—	—	Angiography; ventriculography	None	Unknown/butterfly-like lesions
Shankar/1978	—	—	—	None	Died/bifrontal midline
Letendre/1982	—	—	CT scan	WBR (4,000 rad)	Alive after 24 mo/bifrontal
Mendenhall/1983	80/M	Hemiparesia; hallucinations	—	None	Died after 1 mo/bifrontal
Helle/1984	50/M	Personality changes; papilledema	CT scan	WBR (5,000 rad)	Lost to follow-up/bifrontal
Valderrama/ present case	70/F	Personality changes; confusion	CT scan	WBR (1,300 rad)	Died after 18 d/bifrontal corpus callosum

* WBR = whole brain radiation.

sis is suggested.[21] This is an important distinguishing feature from a cerebral abscess, especially with the rather high frequency of lymphomas and inflammatory processes in immunocompromised patients. The avascularity of the lesions on angiogram[6,20] sets them apart from glioblastoma multiforme and medulloblastoma, as well as metastatic tumors.[20,22]

The recommended treatment for primary CNS lymphomas is whole brain irradiation to 5,000 rad or more, followed by a booster of 500 to 1,000 rad to the site of the tumor.[2,5,6,23] In view of frequent relapses of the tumor in primary or distant sites, it is speculated that the spread of the tumor is by way of the CSF, especially in those cases where the tumor has a subcortical or parameningeal location. It should be noted, however, that cytology is frequently negative prior to surgery. Dissemination may also result from spillage of tumor cells during surgical manipulation. Gonzalez and Schuster-Uitterhoeve,[23] in a review of the literature, found that 26% of the cases had a positive CSF or relapse in the spine following surgery or irradiation. For these reasons, spinal irradiation to a dose of 3,000 to 3,500 rad is recommended.[5,6,23]

Although primary CNS lymphomas are highly sensitive to radiotherapy, long term results are disappointing. Of 150 cases reviewed by Littman and Wang[2] only six cases (4%) were disease free after five or more years. In the majority of patients, the quality of life after radiotherapy is severely impaired. Patients with severe intellectual deterioration at the time of diagnosis will not benefit from aggressive therapy since the cerebral damage is likely to be irreversible. Habib and colleagues[24] obtained a favorable response in a bioccipital lymphoma with a "no touch CO_2 laser procedure." This procedure produced minimal trauma to the surrounding brain.

Chemotherapy has not been recommended for the treatment of CNS lymphomas because of poor penetration of these agents through the blood-brain barrier. In an interesting study, Neuwelt and associates[25] treated three patients with a high dose of methotrexate followed by leukovorin rescue. The drug was administered after the osmotic blood-brain barrier was breached by infusions of mannitol. The patients showed rapid decrease in size and then complete disappearance of the tumor as visualized by CT scans at nine and 16 months after the initiation of therapy.

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Non-Meckelian diverticulosis of the jejunum and ileum: A report of four cases, one with an arteriovenous malformation

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Although diverticula of the jejunum and ileum are usually regarded as innocuous, as are their colonic counterparts, they too are subject to acute and chronic complications. Acute complications such as intestinal obstruction, diverticulitis with or without perforation, and hemorrhage are seen in from 6.5 to 10.4% of patients.[1,2] However, chronic symptoms of intermittent abdominal pain, flatulence with episodes of diarrhea, and malabsorption are reported to occur in from 19.4 to 28.7% of patients.[1,3] Carcinoma of the small intestine in association with diverticulosis has also been reported,[4,5] but is rare.

Four cases of non-Meckelian diverticula of the jejunum and ileum are presented together with a brief review of the literature.

CASE REPORTS

Case 1. A 58-year-old woman was seen in 1973 because of crampy abdominal pain with abdominal bloating and episodes of diarrhea. A complete physical examination was unremarkable with the exception of myasthenia gravis that she was known to have for 30 years. An opaque enema study revealed sigmoid diverticulosis. A complete blood count was normal, as well as upper gastrointestinal series with small bowel follow through.

The patient returned in 1983 with increasing frequency of the abdominal symptoms. On examination she was found to be anemic with a hemoglobin of 10.6 g/dL and a hematocrit of 32%. A small bowel series revealed extensive diverticulosis of the jejunum and ileum (Fig 1). Stools were negative for blood. Further investigation revealed evidence of malabsorption of B_{12}, D-xylose, and fat. The patient was treated with hematinics and intermittent courses of oral tetracyclines and has remained relatively symptom free for the past year.

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FIGURE 1. Roentgenogram of small intestine following ingestion of a barium meal, showing multiple diverticula of the jejunum and ileum.

Case 2. An 88-year-old woman was hospitalized for gastrointestinal bleeding. On admission the hemoglobin was 9.2 g/dL and the hematocrit was 28%. An emergency colonoscopy revealed extensive diverticulosis and evidence of supracolonic bleeding. Gastric endoscopy was negative. Because of a pre-existing ovarian malignancy with metastases, only supportive measures were offered. The patient died after five days and at autopsy was found to have jejunal diverticulosis involving 40 cm of the intestine distal to the ligament of Treitz and an arterial erosion in one of the diverticula.

Case 3. A 71-year-old man was hospitalized because of shortness of breath on exertion. The patient reported having dark stools for approximately two months; he had had peptic ulcer disease that was treated in 1956.

On examination the patient was obviously anemic. A complete blood count on admission revealed a hemoglobin of 5.1 g/dL, a hematocrit of 16.8%, and a red blood cell count of $2.03 \times 10^6/\mu L$. He was treated with a transfusion of packed red cells.

Six days after admission the patient suddenly passed several liquid bowel movements consisting of tarry, foul smelling stools as well as fresh blood. His condition rapidly deteriorated with a precipitous fall in blood pressure. At laparotomy the upper jejunum was found to be the source of bleeding. There was extensive diverticulosis extending from 15 cm distal to the ligament of Treitz, including an 85 cm segment of jejunum. Resection of the affected segment with end-to-end anastomosis was performed.

The patient's postoperative course was uneventful and there has been no further bleeding or other sequelae over a follow-up period of eight years. On examination the resected specimen (Fig 2) revealed an arteriovenous malformation measuring 1.5 cm in diameter that was confirmed on microscopic examination (Fig 3). The arteriovenous malformation was found in the upper jejunum but did not arise from a diverticulum. Even though arteriograms were not performed, a mucosal erosion overlying the malformation was strongly suspected as the cause of bleeding. The remainder of the resected specimen showed extensive diverticulosis but intact mucosa.

Case 4. An 85-year-old woman with diabetes mellitus presented with a complaint of postprandial colicky abdominal pain with bloating and diarrhea for two months. On examination she was found to have a moderately distended but soft abdomen. A complete blood count and SMA-17, as well as serum folate, B_{12}, and carotene were within the normal ranges. Stool specimens were

FIGURE 2. Surgical specimen showing multiple diverticula along the mesenteric border of the jejunum.

FIGURE 3. Case 3. Arteriovenous malformation of the jejunum. (Hematoxylin and eosin stain; original magnification × 70.)

negative for blood. Scout films of the abdomen showed few air-fluid levels without evidence of obstruction. A complete gastrointestinal series showed diverticulosis of the jejunum as well as ileum (Fig 4) over and above that of the sigmoid colon. The patient has been treated conservatively and has run a benign course for the past 18 months of follow-up.

Discussion

The increased frequency of diverticular disease of the small intestine in older patients and the absence of a muscle layer within the intestinal walls has led most authors[3,4,6] to agree that non-Meckelian small intestinal diverticula are acquired pulsion diverticula. Altemeier and associates[2] demonstrated muscular thickening and disturbed peristalsis in the involved segments of the intestine. This finding suggests that disturbed motor activity analogous to that implicated in the pathogenesis of Zenker's diverticulum of the esophagus and diverticulosis of the sigmoid colon may also play a role in the genesis of the diverticulosis of the jejunum and ileum. Benson and colleagues[5] reported colonic or esophageal diverticula in 38% of patients studied who had non-Meckelian diverticula of the small intestine.

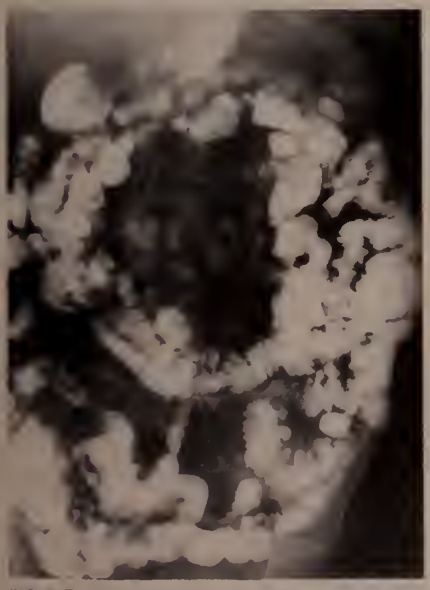

FIGURE 4. Roentgenogram of the small intestine following ingestion of an opaque meal, showing extensive diverticulosis of the jejunum and ileum.

Krishnamurthy and associates[7] demonstrated microscopic evidence of abnormalities of the smooth muscle and the myenteric plexus of the intestinal wall in patients with non-Meckelian diverticulosis. They reported fragmented and degenerated muscle cells that gave a vacuolated appearance to the muscle layers, degeneration of the neurones and axons of the myenteric plexus, and fibrosis of the circular as well as longitudinal muscle layers of the intestine. The authors concluded that diverticulosis of the small intestine is simply a manifestation of an abnormal intestinal wall and ineffective and uncoordinated motility.

Diverticulosis of the small intestine is infrequent; the incidence is reported to range from 0.26% to 1.3% of all autopsy reports.[2,8] It occurs primarily in patients over the age of 60 years, although Khatri and associates[9] have reported four patients who were all under the age of 45 years. Although generally considered innocuous, acute and often life-threatening complications do occur. Prior to the 1960s these diverticula were believed to be largely asymptomatic, but recent clinical studies suggest the opposite. Cooke and coworkers[10] studied 33 hospitalized patients with jejunal diverticulosis and found that all but four of them had either symptoms or metabolic defects attributable to diverticulosis. Nobles[11] emphasized that the triad of obscure abdominal pain, anemia, and dilated loops of jejunum should alert the clinician to the possibility of diverticulosis.

The large ostium and fluid contents of the small intestine make conditions unsuitable for prolonged retention of material within the lumen and for inspissation. However, ineffective peristalsis often leads to the stagnant loop syndrome, bacterial overgrowth, and malabsorption characterized by high serum folate levels, megaloblastic anemia, and steatorrhea. An overgrowth of coliform organisms in the small intestine leads to the deconjugation of bile acids and the intraluminal metabolism of vitamin B_{12}. With the establishment of steatorrhea, superimposed deficiencies of fat soluble vitamins may occur. The diagnosis is established by measurements of serum folate, vitamin B_{12}, and carotene and the use of the D-xylose absorption and Schillings tests. The identification of coliform organisms in the proximal intestinal aspirate is also useful. Treatment consists of therapy with antimicrobial agents given intermittently on a rotation schedule in order to combat bacterial overgrowth and also to prevent the emergence of drug-resistant strains. Commonly used agents include the oral administration of tetracycline, clindamycin, ampicillin, and metronidazole. Clinical response as well as a normal bile salt breath test are utilized as guides to the effectiveness of the antibiotic regimen.

Larger diverticula full of contents may appear as air-fluid levels on scout films and may be mistaken for an intestinal obstruction. On the other hand, however, large diverticula may cause true obstruction and even volvulus from the sheer weight when full, especially in the face of a high fiber diet.

Diverticulitis per se is a rare complication, as is bleeding. Prior to 1971 fewer than 40 cases of major gastrointestinal hemorrhage from jejunal diverticulosis were reported in the English language literature.[11] However, to our knowledge, massive hemorrhage from an arteriovenous malformation of the jejunum in association with diverticulosis of the small intestine (Case 3) has not been reported before. Four cases of non-Meckelian diverticula of the jejunum and ileum have been presented above. This entity is uncommon but awareness of it on the part of physicians may result in many more cases being recognized.

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Diagnosis of pulmonary toxoplasmosis by bronchoalveolar lavage

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Toxoplasmosis is an opportunistic infection that occurs in immunosuppressed patients. However, the serologic diagnosis of acute toxoplasmosis may be unreliable or difficult to interpret in certain immunocompromised patients, such as those with the acquired immunodeficiency syndrome (AIDS),[1,2] organ transplants,[3] or cancer.[4] Demonstration of trophozoites in tissue or body fluids is definitive proof of acute toxoplasmosis.[5] Fiberoptic bronchoscopy (FOB) and bronchoalveolar lavage (BAL) have been demonstrated to be useful techniques for the initial evaluation of the immunosuppressed patient with new pulmonary infiltrates,[6] but only rarely has toxoplasmosis been diagnosed by this technique.[7] The following is a report of a case of an immunocompromised bone marrow transplant recipient with fever and new infiltrates in whom a diagnosis of pulmonary toxoplasmosis was proven by BAL.

CASE REPORT

A 23-year-old man with chronic myelogenous leukemia diagnosed in November 1983 received a bone marrow transplant from an HLA-matched sibling in June 1984. Prior to transplantation, he received two doses of cyclophosphamide (60 mg/kg) and 1,200 rad of total body irradiation administered in a hyperfractionated schedule. The patient was maintained on cyclosporine for immunosuppression. He experienced several febrile episodes including two documented episodes of staphylococcal septicemia and one episode of candida sepsis that were treated successfully with antimicrobial agents. After the transplant the patient experienced a successful engraftment; however, he then developed pancytopenia.

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In December 1984, the patient received a second bone marrow transplant from the same HLA-matched sibling. Methotrexate was administered for prophylaxis against possible graft-versus-host disease (GVHD). The patient experienced another febrile episode of unknown origin that was treated with broad spectrum antibiotics without success. Multiple cultures were negative. An IgG enzyme linked immunosorbent assay (ELISA) for *Toxoplasma gondii* was moderately positive (titer 1/16 to 1/64), but the IgM-fluorescent antibody was negative. The patient then experienced nonproductive cough and progressive dyspnea. Arterial blood gas studies revealed significant hypoxemia while breathing room air (pH, 7.43; P_{CO_2}, 26; P_{O_2}, 53). Empiric broad spectrum antibiotic therapy with cefoperazone, amikacin, acyclovir, trimethoprim-sulfa, and erythromycin was initiated. Supplemental oxygen and corticosteroids were also administered, and methotrexate was discontinued. The patient became more dyspneic; the arterial blood gases deteriorated such that assisted ventilation was required.

The fever persisted and new bilateral pulmonary infiltrates were seen on chest roentgenogram. The total WBC count was 1,300/μL; the platelet count was 16,000/μL. FOB was performed because of persistent fever, dyspnea, and progressive pulmonary infiltrates.

The FOB, performed via the endotracheal tube while the patient was on mechanical ventilation, revealed normal endobronchial anatomy. The bronchoscope was wedged in a segmental orifice of the right-middle lobe and the lobe lavaged with five 30 cc-aliquots of normal saline. The bronchoalveolar lavage specimen was divided and sent for bacterial, viral, fungal, and mycobacterial cultures. A specimen of the BAL was centrifuged, and smears of the sediment were stained with silver-methenamine, acid-fast, Gram, and Giemsa stains. All of the stains and cultures were negative, except for the *Toxoplasma gondii* seen in the lavage specimen stained with Giemsa (Fig).

The patient was treated for toxoplasmosis for three weeks with intravenous trimethoprim-sulfa. He became afebrile and less dyspneic three days after the initiation of the medication. After eight days of therapy, the patient was successfully removed from assisted ventilation, and after 18 days of therapy the chest roentgenogram was normal. Oral sulfadiazine was then initiated, but was discontinued after only 12 days because of progressive leukopenia. Pyrimethamine was not given because of the possibility of drug-induced bone marrow toxicity. The broad spectrum antibiotics were continued for two weeks after the FOB, until all of the cultures were reported as showing no growth. The patient remained afebrile.

FIGURE. Crescentic blue staining trophozoites of *T. gondii* as seen in BAL sediment stained with Giemsa stain. (Approximate original magnification ×1,000).

Two months later the patient once again became febrile, dyspneic, with new pulmonary infiltrates, and died within 24 hours. Autopsy revealed extensive pneumonia and pulmonary hemorrhage. Pseudocysts of *T. gondii* were seen on both hematoxylin-eosin and Giemsa-stained lung sections. Giemsa-stained touch preparations of the lung and liver showed typical trophozoites of *T. gondii*. Viral cultures of lung tissue grew cytomegalovirus (CMV). Silver-stained lung tissue did not show any evidence of *Pneumocystis carinii* or fungal infection.

DISCUSSION

Toxoplasma gondii is a ubiquitous obligate intracellular protozoan capable of infecting a wide range of vertebrates, including humans. However, the domestic and feral cats are the definitive hosts. The cat produces resistant oocysts containing infective sporozoites that are passed to the environ-

ment in cat feces and may remain infective in moist soil for weeks. If ingested by humans, tissue invasion and asexual reproduction of the parasite occur. The major routes of transmission of *T. gondii* in humans is congenitally or by ingestion with food. Tissue cysts may be present in meat used for human consumption, and ingestion of oocysts in undercooked meat is a major means of transmission. There is no evidence of direct human-to-human transmission, except mother to fetus. Transfusions of whole blood or WBCs infected with the parasite have resulted in transmission to the recipient.

Antibodies to *T. gondii* are found in 17 to 50% of population groups tested in the United States. Although toxoplasmosis is a common infection, it rarely gives rise to acute disease in the normal host. Acute toxoplasmosis in immunocompromised patients is most likely due to recrudescent rather than primary infection.[8] Toxoplasmosis is often associated with other opportunistic infections; concomitant infection with DNA viruses is especially common.[5,10] Neurologic involvement occurs in the majority of cases.[9] Lung tissue in patients with pneumonitis caused by *T. gondii* may show an interstitial inflammation or focal bronchopneumonia. Intracellular protozoa may be seen in alveolar macrophages. Pseudocysts, cysts, and proliferative forms of *T. gondii* may be seen in alveolar lining cells or in alveoli themselves.

Bronchoalveolar lavage is a safe diagnostic procedure for use in patients with pulmonary disease. In a group of immunosuppressed patients with diffuse pulmonary infiltrates, BAL had an overall diagnostic yield of 66%. It was most effective in the diagnosis of opportunistic infections, including *Pneumocystis carinii*, CMV, fungal pneumonia, and mycobacterial disease.[6] In human bronchoalveolar lavage fluid, the trophozoite is a crescentic or oval body and 5 to 7 μm by 2 to 4 μm in size; it stains blue with a reddish nucleus in Giemsa or Wright stain (Fig). The organism may be seen intracellularly or may be found free, as was seen in this case. The BAL sediment must be carefully searched because the organism may be confused with cellular stroma or debris.

Toxoplasmosis is a potentially curable opportunistic infection. However, the diagnosis is often only made at autopsy.[7] Serologic tests may be unreliable or difficult to interpret in immunosuppressed patients, and it may be difficult or impossible to perform appropriate biopsies in patients who are acutely ill or have abnormal bleeding parameters.[7] FOB and BAL may usually be performed in these patients. If toxoplasmosis is considered in the differential diagnosis, Giemsa stains of the BAL sediment may be searched for trophozoites of *T. gondii*. Although the sensitivity of BAL in determining toxoplasmosis is unknown, awareness that it may be diagnosed in this manner may permit this potentially curable illness to be identified and treated in immunosuppressed patients.

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See also pp 171–172.

Metastatic Kaposi's sarcoma and bilateral chylothorax

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There have been numerous recent reports of disseminated Kaposi's sarcoma in homosexual men.[1,2] The clinical features, natural history, and mortality of the disease in homosexuals are similar to the disseminated form seen in Africa and in immunosuppressed renal transplant patients.[1] The following case report describes a homosexual patient with metastatic Kaposi's sarcoma and bilateral pleural effusions. Initially, the effusions were nonchylous and related to direct pleural involvement by the tumor. However, the patient subsequently developed massive bilateral chylothoraces, a previously unreported occurrence under such circumstances.

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Case Report

A 36-year-old homosexual man presented to The Presbyterian Hospital in New York City in September 1984 complaining of dyspnea on exertion. Physical examination revealed dullness at the base of the left chest and purple-black nodules on all four extremities. The patient was anergic and skin biopsy demonstrated Kaposi's sarcoma. Chest

TABLE. Pleural Fluid Laboratory Data in a Patient with Metastatic Kaposi's Sarcoma

	September 1984	January 1985
Protein (mg/dL)	5,870	5,760
Glucose (mg/dL)	96	123
Cholesterol (mg/dL)	67	76
Triglycerides (mg/dL)	53	893

film showed a moderate left pleural effusion, a small right effusion, normal heart size, clear lungs, and no pulmonary vascular congestion. Thoracentesis yielded 400 cc serosanguineous nonchylous fluid (Table). Cytology and cultures of the fluid were negative. Repeated percutaneous pleural biopsies showed nonspecific pleural inflammation. Fiberoptic bronchoscopy demonstrated normal airways and there was no evidence of opportunistic infection based on bronchoalveolar lavage and transbronchial biopsy. A computed tomography (CT) scan demonstrated small bilateral effusions, no gross mediastinal masses or adenopathy, and no parenchymal lung disease. Bilateral areas of posterior pleural thickening up to 8 mm were noted. The patient underwent a left thoracotomy at which time the lung and pleura appeared grossly normal. Biopsy of the pleura revealed mild inflammation and focal thickening by a nodular, poorly-circumscribed aggregate of spindle cells. Interspersed among these cells were many small slit-like spaces containing red blood cells. Numerous extravasated red cells were also present. The appearance was consistent with Kaposi's sarcoma involving the pleura (Figure). The patient underwent pleurodesis

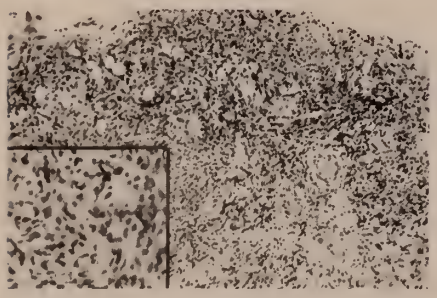

FIGURE. This view of the pleural biopsy shows a spindle cell proliferation in pleural tissue. Numerous vascular slits are seen within the tumor. Inset: a high power view illustrates the bland cytologic features and vascular channels (between arrows). (Hematoxylin-phloxine-saffranin stain; original magnification × 100, inset × 250).

with local instillation of tetracycline and began a chemotherapeutic regimen of vinblastine and bleomycin. The skin lesions regressed and the left effusion did not recur.

The patient was readmitted to the hospital in January 1985 with worsening dyspnea, cough, and fever. Physical examination demonstrated extensive chest dullness bilaterally and recrudescence of skin lesions. Chest film revealed massive bilateral effusions with fluid at the level of the fourth rib posteriorly. There was diffuse interstitial involvement of lung fields. Bilateral thoracenteses yielded 1 L of milky white fluid that remained opaque after standing overnight. Laboratory analysis confirmed the chylous nature of the fluid (Table). Cytology and cultures of the fluid were negative. Bronchoscopy demonstrated mildly erythematous airways but no endobronchial lesions. Transbronchial biopsy revealed both pneumocystis and cytomegalovirus infection. Bilateral effusions with bilateral lower lobe atelectasis were seen on CT scan, but no mediastinal masses or adenopathy were noted. The patient was treated with trimethoprim-sulfamethoxazole, bilateral chest tubes, and parenteral hyperalimentation. He defervesced and his respiratory status improved. The patient underwent repeat tetracycline pleurodesis and his chemotherapeutic regimen was switched to actinomycin D and VP-16. Despite these measures, the pleural fluid reaccumulated and the chest tubes were reinserted. The patient subsequently developed progressive respiratory failure and died. Permission for autopsy was denied.

Discussion

This case report describes two relatively common mechanisms of neoplasm-related pleural effusion in the setting of a previously uncommon metastatic tumor. The first mechanism involves direct neoplastic involvement of the pleural surface. Metastatic Kaposi's sarcoma has been reported to involve the pleura clinically,[2] and on postmortem examination.[3-5] These cases, however, were associated with concomitant lung involvement or with widespread visceral metastases. In contrast, the patient reported here presented with symptoms referable only to pleural involvement without evidence of pulmonary parenchymal disease or extensive visceral metastases.

The second mechanism of malignancy-related pleural effusion demonstrated by this case presumably involves the obstruction of the thoracic duct by the neoplasm, allowing for the leakage of chyle into the pleural spaces with resultant bilateral chylothorax. Other known causes of bilateral chylous effusions, including trauma and surgical interventions, were not present. Our conclusion that the pleural fluid during the second admission was truly chylous is based on the very high level of triglycerides, as described by Staats and associates.[6] The chylous effusions occurred despite the patient's malnourished status (when the fat content of the thoracic duct lymph is low and the effusion may appear serous) and persisted with parenteral hyperalimentation.

Lymphomas account for the majority of malignancy-related chylothoraces, with other neoplasms occasionally involved. This case represents, to our knowledge, the first reported occurrence of metastatic Kaposi's sarcoma and bilateral chylothorax. We anticipate that with the rising incidence of Kaposi's sarcoma and the acquired immune deficiency syndrome there will be an increasing number of patients who present solely with symptoms referable to pleural disease.

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ERRATUM

On the cover of the February 1986 issue of the *Journal*, a line of authors names was inadvertently dropped from the Table of Contents. The authors for the article entitled, "Results of a public screening program for colorectal cancer," are as follows: K. Michael Cummings, PhD, MPH, Arthur Michalek, PhD, John Tidings, Lemuel Herrera, MD, Curtis Mettlin, PhD.

Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

Sequential bilateral germ cell tumors of the testis

TO THE EDITOR: In April 1976 a 20-year-old man presented with a two-month history of left testicular pain and swelling. A left radical orchiectomy revealed a malignant teratoma with foci of seminoma, embryonal carcinoma, and choriocarcinoma. A retroperitoneal lymph node dissection of 33 nodes was negative for metastases. Considered in Stage IA, the patient received adjuvant chemotherapy consisting of vinblastine sulfate, actinomycin, and chlorambucil between June 1976 and July 1977 for six months. His alpha fetoprotein and human chorionic gonadotropin levels were always negative as well as follow-up chest radiographs. Eight years later in July 1984 the patient was found to have a right testicular seminoma diagnosed after right radical orchiectomy for a testicular mass. Abdominal and pelvic computed axial tomography scans were normal as were markers taken prior to orchiectomy. The patient was referred for adjuvant radiotherapy and is presently being maintained on oral testosterone.

Germ cell tumors of the testis are rare, generally occurring in 2 per 100,000 men. A second primary germ cell tumor, either coexistant or sequential, occurs in 1 to 3% of these patients. Although this condition is rare, the purpose of this communication is to remind the medical community that one should not consider a cancer patient cured regardless of the time elapsed since the initial presentation of the condition.

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Gastrointestinal hemorrhage caused by colonic varices

TO THE EDITOR: We read with interest Canver and Upson's article entitled, "Massive lower gastrointestinal hemorrhage secondary to colonic varices" (1985; 85:604-605). A similar patient was reported by us in 1978. A 52-year-old man presented with copious bright red rectal bleeding.[1] The patient had a diagnosis of Laennec's cirrhosis as determined on biopsy. Upper endoscopy was completely normal. Colonoscopy was unsuccessful because of the excessive bleeding and a barium enema was nondiagnostic. Because of arterial hemorrhage the patient underwent an exploratory laparotomy. At surgery splenic flexure varices were found originating from the lower pole of the spleen. A left hemicolectomy was performed. The patient developed a severe coagulopathy postoperatively and died.

We would like to make three points. Abnormal venous collaterals between the spleen and splenic flexure of the colon exist and may cause colonic variceal hemorrhage. According to Edwards,[3] these collaterals originate in the embryo from the juxtaposition of developing systemic and visceral venous plexuses.

The second point we would like to make is that colonic varices may occur in patients who do not have esophagogastric varices.

Thirdly, the treatment of choice for variceal bleeding is portasystemic shunting. This not only deals with the acute problem, but prevents the further development of variceal collaterals.

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In reply: We are pleased to respond to the comments by Drs Freed and Reiner. As we stated in our article, the most significant portasystemic collateral anastomosis is between the left gastric and coronary veins and the azygos system via the esophageal veins. Utilizing splenoportography, Britton[1] showed that esophageal collaterals are the primary anastomotic channels in at least one half of all patients with portal hypertension. The other main channel is the inferior mesenteric left iliac venous system. This system is involved as a primary collateral in about one third of patients treated.

We also agree with the third point made. Despite the fact that no long-term follow-up is available, it appears that portacaval shunting is safer in the short term for massive variceal bleeding. With primary portal decompression, resection of unprepared bowel with its attendant morbidity is avoided. The advantages of a shunt procedure outweigh the potential disadvantages.

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Fungal infection masquerading as acute pulmonary embolization

TO THE EDITOR: Localized sharp pleuritic chest pain, mild shortness of breath, a fall in arterial PO_2, and a clear chest roentgenogram in six patients with neutropenic acute leukemia led us to search aggressively for the presence of pulmonary emboli. However, following empirical therapy with heparin as well as diagnostic procedures such as lung scans and pulmonary angiograms in two out of six patients, it became apparent that they had large cavitating

TABLE. Clinical and Laboratory Characteristics of Patients with Neutropenic Acute Leukemia and Pulmonary Fungal Infections

Patient	Age	Diagnosis	Chest pain Side/Intensity	PO_2 (mm Hg)	Chest film	Lung scan	Pulmonary angiogram	Procedure	Diagnosis
#1	49	AML†	Right/4+	54.8	Clear → right basilar infiltrate	—	—	Thoracotomy	Aspergillosis
#2	19	ALL	Left/4+	51.0	Clear → left-upper lobe fungus ball	Several matched ventilation/perfusion defects	Negative for embolism	Thoracotomy	Mucormycosis
#3	74	AML	Left/4+	72.0	Clear → left-mid-lung infarction	Normal	Negative for embolism	Autopsy	Aspergillosis
#4	49	AML	Right/2+	—	Clear → several patchy infiltrates → well defined densities	—	—	Bronchoscopy	Candidiasis
#5	69	Blastic crisis of CML†	Left/3+	—	Clear → bilateral nodular infiltrates	—	—	Autopsy	Trichosporin
#6	21	AML	Right/4+	133.6	Clear → cavitating ball in right lower lobe	—	—	Thoracotomy	Mucormycosis

The bone marrow status for all patients was hypoplastic from chemotherapy.
* AML = acute monocytic anemia.
† CML = chronic monocytic anemia.

fungal lesions in the chest. The purpose of this report is to alert the medical community to the possible initial mode of presentation of fungal infections as pulmonary emboli.

Six patients rendered severely neutropenic (WBC count less than 100×10^9/L) by chemotherapy became febrile. Therapy with a combination of an aminoglycoside and a semisynthetic penicillin was promptly instituted. During this period of hypoplasia, each of the patients developed localized sharp, pleuritic chest pain. The severity ranged from moderate (2^+) to excruciating (4^+) pain that was aggravated by deep inspiration. In four cases, arterial blood gases were obtained immediately, and three patients had lower than expected PO_2 values (Table). Physical examination in four of the six cases revealed a localized pleural friction rub over the area of pain that disappeared during the ensuing 24 to 48 hours. Chest roentgenograms in every case failed to show any abnormality. Given these findings, three patients were empirically treated with heparin, and two had further evaluation with lung scans and pulmonary angiograms, the latter studies failing to demonstrate the presence of pulmonary embolization.

Within a week of the symptoms, large cavitating lesions developed on the chest roentgenograms in every case. A definitive diagnosis of fungal infection was established in each case; three by thoracotomy, one by bronchoscopy and biopsy, and at autopsy in two patients who died soon after the onset of symptoms. There were two cases of mucormycosis, two cases of aspergillosis, and one case each of trichosporon and candidiasis. Amphotericin B (0.6 mg/kg) was administered intravenously to each patient, providing a total dose of approximately 2.5 to 3.0 g. Two cases (patients 3 and 5) died within two weeks of developing symptoms. Three patients lived for three to 12 months before succumbing to their leukemias, and one patient (6) is still alive and receiving antifungal therapy following thoracotomy.

The course of fungal invasion, which most likely accounts for the symptoms resembling pulmonary infarction, has been previously described in the literature.[1] The invading fungus initially involves the arteries, causing peripheral infarction and organization of the "fungus ball" in the necrotic area. At this stage, control and resolution of the infection by antifungal agents alone, which are probably prevented from reaching the involved area due to necrosis, is highly unlikely.[1] It is imperative, therefore, that early recognition and empirical therapy, if necessary, be practiced by alert physicians involved in such cases.[2]

Empirical intervention with broad spectrum antibiotic therapy in febrile, neutropenic patients has resulted in a dramatic decline in mortality from bacterial infections.[3-5] We anticipate similar results by instituting antifungal therapy at a time when the inoculum size of the invading fungus is still low and when tissue or visceral invasion has not yet occurred.[6]

In conclusion, we are witnessing a new and unexpected presentation of invasive and aggressive fungal infection, whose recognition is crucial so that early therapeutic intervention may be instituted. In addition, we strongly advocate the empirical use of amphotericin B in such high risk patients.

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Calcified gallbladder and peritonitis in a newborn

TO THE EDITOR: Calcified gallbladder and fetal cholecystitis are extremely rare diseases in the newborn. However, chemical peritonitis with superimposed bacterial infection is found somewhat more frequently in this age group. All of these entities were present in the patient under discussion. Although the pathogenesis of some of these illnesses in the perinatal period is not clearly established, comparison with the cause and mechanism of similar diseases in young infants is useful.

Case Report. A male newborn weighing 2466 g was delivered vaginally at 38 weeks gestation. The obstetrician diagnosed hydramnios. Physical examination at birth revealed no abnormalities. The infant accepted formula and passed meconium. At the age of 39 hours, he started to vomit yellow fluid and his abdomen became distended. On radiographic examination a large, ring-shaped calcific density was seen in the right upper quadrant (Fig).

An exploratory laparotomy was performed four days after birth. Diffuse peritonitis and abundant fibrinopurulent exudate were present in the abdomen. Numerous fibrous adhesions with a small amount of calcification connected the distal ileum with a partially calcified gallbladder. There was a volvulus of the ileum at the site of the adhesions. A small perforation was noted in the gallbladder and another in the ileum after these two structures were separated. The portion of the intestine with the perforation was resected. Because of massive adhesions, further dissection of the gallbladder was dangerous; for this reason, only a biopsy and cholecystostomy were performed.

The postoperative course was satisfactory. Culture of the peritoneal exudate revealed the presence of *Escherichia coli* and coagulase negative *Staphylococcus aureus*. The infant was therefore treated with appropriate antibiotics. Serum calcium and phosphorus levels were normal. Histologic examination of the gallbladder wall revealed acute and chronic suppurative inflammation with areas of calcification.

The infant made a satisfactory recovery and the cholecystostomy tube was removed prior to discharge. The infant was followed in the office for eight years during which time his growth and general health were good.

Discussion. It is evident that this patient had cholecystitis with calcification. In the case of dystrophic calcification, the damaged tissue will be faintly calcified four to nine days after the injury, and the calcification will be prominent three weeks after the onset of the illness.[1] In the patient discussed here, marked calcification of the gallbladder wall was noted two days after birth. Therefore, the cholecystitis started during fetal life at least two weeks before birth. Information on fetal cholecystitis could not be found in the literature, and the cause of this condition in the fetus is not known. Cholecystitis in infants and children may be caused by several pathologic processes. Congenital abnormalities of the cystic duct including atresia, stenosis, cholangitis and other inflammatory processes, edema of the cystic duct, and its compression by enlarged lymph nodes have been described in association with cholecystitis.[2,3]

FIGURE. A frontal view of the chest and abdomen shows a calcific density in the right upper abdominal area (left); a lateral view reveals the ring-shaped calcific density in the anterior abdominal area.

In newborns, dystrophic calcification is found in many organs—bowel, liver, myocardium, arteries, undescended testicles, and the urinary bladder. However, calcification of the gallbladder in a newborn has not been described in the medical literature, although numerous articles are published about the calcification of this organ in adults. Dystrophic calcification—formation of hydroxyapatite in damaged tissues—begins in the mitochondria or in the nonmitochondrially-derived membrane fragments, analogous to matrix vesicles.[4] Once a few mineral crystals are generated, the calcification proceeds by the deposition of calcium and phosphate from the metastable extracellular fluid.

Although the most prominent finding in the patient described here was the calcified gallbladder, fetal peritonitis was also present.

The most common inflammatory process of the peritoneum during intrauterine life is meconium peritonitis. This illness is caused by the passage of meconium through a perforation of the bowel into the peritoneal cavity. Digestive enzymes present in the meconium produce severe inflammation of the peritoneum with numerous fibrous adhesions and small areas of calcification scattered throughout the abdomen. In this patient, the calcification was limited to the gallbladder area, and, except for the fibrous adhesions, the biopsy specimen did not show any element observed in meconium peritonitis. It is possible, however, that during fetal life this patient had a perforation of the ileum with fistulization to the gallbladder. This pathology would produce a seepage of intestinal contents into the peritoneal cavity, causing a localized meconium peritonitis.

Biliary peritonitis is a rare cause of peritoneal inflammation in a newborn infant. This illness is produced by spontaneous perforation of the common bile duct distal to the entry of the cystic duct.[5,6] It is probable that in this patient the fundus of the gallbladder perforated as a result of cholecystitis during intrauterine life, and its contents drained into the peritoneal cavity, producing bile peritonitis with numerous adhesions between the gallbladder and neighboring structures.

The peritoneal findings in this patient were the result of two diseases. During fetal life, the patient had chemical meconium or biliary peritonitis, and after birth the ileal perforation caused acute bacterial peritonitis. The culture

of the peritoneal exudate was positive for both *E. coli* and coagulase-negative *S. aureus*. Bacterial peritonitis in the newborn is frequently caused by two or more organisms.[7]

This unusual case presents the rare combination of separate prenatal and postnatal episodes of peritonitis, as well as the unique finding of a neonatal calcified gallbladder.

Acknowledgment. The authors thank Dr Stanley S. Friedman for his assistance in the preparation of this letter.

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Long-term neurologic complications of metoclopramide

TO THE EDITOR: Metoclopramide, which is frequently prescribed for a variety of gastrointestinal symptoms including nausea, vomiting, flatulence, dyspepsia, and delayed gastric emptying, is known to have neurologic side effects.[1] Various extrapyramidal syndromes have been described, including Parkinsonian signs, acute dystonic reactions, and tardive dyskinesias.[2] The following is a report on the case of an elderly patient who developed Parkinsonian signs on metoclopramide and permanent tardive dyskinesia after its withdrawal.

Case Report. An 84-year-old woman had been taking diazepam 10 mg a day for 20 years for anxiety. Metoclopramide was prescribed by her family physician for symptoms of epigastric pain from March until October 1984. Within a few months of starting the medication she noted stiffness of her legs and difficulty walking. She also complained of clumsiness of her hands in performing fine tasks. These symptoms were first noted in the spring of 1984 and gradually worsened. Tremor of the hands was noted in July 1984.

A neurologic examination in October 1984 revealed an alert woman with no significant impairment of intellectual abilities. She had facial rigidity, a positive glabella sign, and rigidity at both wrists and elbows with bilateral resting tremor of all extremities. Her gait was rigid with a tendency to shuffle and with no swinging of either arm. These symptoms and signs were assumed to be the result of metoclopramide therapy; the medication was therefore discontinued. The patient's symptoms rapidly disappeared within four to eight weeks. Within a week or two of discontinuing the metoclopramide, her daughter noted some involuntary movements of the mouth, including continuous lip smacking and tongue motions that reached a peak within a few weeks after discontinuing the medication. These improved minimally, but persisted when last seen six months later.

Discussion. Extrapyramidal reactions from metoclopramide tend to occur in 1 in 500 patients.[3] These include acute dystonic reactions that may occur early in the course of treatment and clear promptly once the drug is stopped. They are more often seen in younger patients and in children and may take the form of akathisia or spasmodic deviation of the eyes, head, or hands. Parkinsonism develops after weeks to months on metoclopramide and is seen more frequently in older patients[2]; it is gradually reversed by withdrawal of the drug.

A third movement disorder that may follow the long-term use of metoclopramide is tardive dyskinesia or orofacial dyskinesia. This is a potentially irreversible side effect and is seen in one in 1,000 patients over the age of 70.[4] It may develop while the patient is taking the medication, or only after its withdrawal. This reaction is identical to that which develops after the long-term use of phenothiazines or butyrophenones. It has been hypothesized that tardive dyskinesia is probably due to dopamine hypersensitivity resulting from receptor deprivation by long-term antagonist usage, with the D1 receptor being blocked by phenothiazines or butyrophenones. Metoclopramide may induce this state in relation to the D2 receptor.

The patient described here, as well as those previously reported in the Swedish and Canadian literature, indicate that metoclopramide may produce irreversible tardive dyskinesia. Hence its use for minor symptoms should be avoided, and particular care should be exercised in administering it to older patients.

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HEALING THE WOUNDS. A PHYSICIAN LOOKS AT HIS WORK

By David Hilfiker, MD. 209 pp. New York, Pantheon Books, 1985. $14.95 (hardcover)

This book is an in-depth, personal account of the realities of medical practice in today's world. The author, a family physician, draws on his seven years of rural practice and two years of inner-city work in order to pry open the Pandora's box of a physician's innermost feelings. The current text builds on the springboard of two prior articles in the *New England Journal of Medicine* by the same author. Although there have been similar books dealing with the extraordinary pressures of medicine (*The Making of a Surgeon* by William Nolen; *Vital Signs* by Fitzhugh Mullan; *Awakenings* by Oliver Sachs; and *Recombinations* by Perri Klass), none have synthesized them so well or poignantly as *Healing the Wounds*.

The first chapter entitled "Cardiac Arrest" launches the reader into the intense emotional issues all physicians face during their careers: death, uncertainty, omnipotence, the technologic imperative, and service versus efficiency and productivity. The chapters entitled "The Pressure Cooker" and "The Limits of Help" further develop the intense paradoxical nature of a physician's work: simultaneously serving individual and societal needs by moving from routine to crisis situations and back again; balancing the emotional needs of a patient with the doctor's "gold standard" of compassionate detached concern and matching the physician's personal needs with those of the patient. The three subsequent chapters —"Boundaries of Knowledge," "Uncertainty," and "Mistakes"—drive home the greatest insecurity of a practicing physician, "the fact that medical science is always uncertain and that it is not possible to know what one does not know." During training a definitive diagnosis of disease is considered the expected outcome of good patient management and it is predicted due to an exhaustive work-up and strong differential diagnosis. The discussion of the softer aspects of the patient's illness is often met with resistance on the wards of university medical centers. The practice situation, however, creates an unbearable dilemma since optimal patient care requires consideration of a delicate balance of illness elements (ie, actual pathology, psychosocial considerations).

The following seven chapters discuss specific escape mechanisms regularly used by doctors. Although the physician is the patient's advocate and employee, there are times when the interests of the patient are in conflict with societal good or the physician's personal advantage. Sincere collaboration must then give way to each party's own goals. For example, the ethics of managing the terminally-ill patient is fraught with difficulty. Best interest often becomes a catch-22 for the physician because it is on his or her shoulders that the relief of suffering, quality and length of life, family considerations, costs, and functional preservation must largely fall. The spiraling responses of prestige, authority, heirarchy, wealth, efficiency, productivity, and detached concern thrust the physician into the unwelcome illusion of playing god. However, clinical detachment is a useful protective response that allows a physician to separate from the anger, fear, panic, confusion, and desperation of many medical situations. It also spares the physician from emotional burnout. Unfortunately detachment may lead to escapism, so that medical cases become strictly scientific or technologic curiosities with the emotional elements of illness either nonexistent or very much removed. As the author also notes, such detachment may harmfully spill over into the physician's social life.

Dr Hilfiker points out that the drive to become more productive in the face of diminishing time often consumes a busy practitioner. The element of control is utilized in order to maximize patient and staff efficiency. Ironically, a vicious cycle is created that spills over on the practitioner himself. Important medical arts and human values soon become secondary, and fewer patient needs are actually met. The social and cultural authority of a physician may also impede the delivery of patient care. As society's gatekeeper the physician defines reality and makes value judgments that the patient often will accept as valid. Such a patient-physician heirarchy also extends to the physician-staff relationship. Tests and procedures are ordered; the supporting staff complies. Salaries reflect the disparity. Thus the ideal Hippocratic goals of altruism and service give way to self-interest and entrepreneurship. The physician becomes a wounded healer.

Throughout the text Dr Hilfiker provides actual examples from his practice that buttress and highlight his arguments and presentation. Real life cases strike at the very roots of modern medical practice. Such painful realities led Dr Hilfiker to leave his rural practice of seven years, and after a one year sabbatical, to resume his practice in an inner city clinic where he currently practices. The key issue is that a physician must recognize and accept vulnerability in the healing process, and use this knowledge in order to move ahead in a positive way by ministering to others.

Healing the Wounds is cover-to-cover reading. The message is poignant, sincere, and apropos to all physicians. I highly recommend it.

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THE DIFFICULT CHILD. A NEW STEP-BY-STEP APPROACH BY A NOTED CHILD PSYCHIATRIST FOR UNDERSTANDING AND MANAGING HARD-TO-RAISE CHILDREN

By Stanley Turecki, MD, and Leslie Tonner. 224 pp. New York, Bantam Books, Inc, 1985. $15.95 (hardcover)

"I am a child and family psychiatrist," says Stanley Turecki in the introduction to his book, "and the parent of a difficult child." With that, the theme is set. This is to be a book, anecdotal in nature but also professionally authoritative, directed primarily to parents of difficult children. The professional authority stems from Dr Turecki's experience with 149 families with difficult children referred to the Difficult Child Program that he founded at Beth Israel Medical Center in New York City in 1983 or those he has seen in private practice.

Dr Turecki defines the symptom dimensions of the difficult child and attempts to place these symptoms along a spectrum of temperamental characteristics—genetic traits that underlie behavior—rather than seeing the child as fitting the diagnostic label of "hyperactivity" or "attention deficit disorder." The temperamental characteristics with which he is concerned relate to activity level, distractions, adaptability, approach/withdrawal, intensity, regularity, sensory threshold, and mood. He rightly criticizes the tendency to create a diagnosis on the basis of a characteristic behavioral symptom and, also rightly, he recognizes the many causative factors, other than temperament, that may be implicated in the behavior of the child. For the purpose of this book, however, cause is not his main concern. Dr Turecki is interested in what the behavior of the difficult child does to the child, his parents and siblings, his teachers, his pediatrician; how his temperamental characteristics influence his behavior as he goes through the day at home, at school, at play, and in both new and familiar situations.

Most importantly, however, is his interest with the management of such a child and his family. It is in this section of the book that Stanley Turecki makes a practical contribution. His philosophy is stated "if you can learn to understand your child and his difficult temperament, you will begin to comprehend what is going on with him and your family." Understanding the problem means that the parents must first list the disturbing behavior characteristics of their child and relate those characteristics with situations or settings in which they occur; secondly, relating such behavior patterns to specific temperamental characteristics; and thirdly, understanding how effectively they as parents deal with these behavior characteristics.

However, understanding is only a significant beginning. For those behavior characteristics that do not appear to be based on temperament, behavior modification techniques are recommended, positive management as well as punishment. However, the behavior program for the child is tied to cognitive change in the parents (ie, "think and evaluate, get your feelings out of it, try not to act like a victim"). For those behavior patterns that appear to be based on temperamental characteristics, the approach is to understand that basis. One must then confront the child with a statement indicating that the parent knows and appreciates what the child is feeling and experiencing. An attempt must be made to buffer that temperamental trait by distraction, cooling off, establishing time to let off steam, offering choices, giving the child time to prepare for change, outlining sequences of events, introducing new things gradually, separating bedtime from sleep time and meal time from eating time, making sure the child understands what is wanted, and not challenging sensory thresholds. In short, one must try to understand the behavior patterns that stem from temperamental characteristics; buffer them, support them, and prevent them. For parents, family support groups have proven helpful.

To do all of this is not an easy task. However, Dr Turecki takes parents through the process of their own change slowly, gently, and wisely. His book is written in an easy conversational style that is nontechnical and sprinkled with case vignettes at each step. Suggestions for the exact words and deeds with which to manage specific behavior characteristics are provided. Although the book is written for parents, it may be read with profit by pediatricians, educators, and mental health professionals, including child psychiatrists who may then recommend this book to the parents of a difficult child. Incidentally, Dr Turecki's own difficult child, age 11 years when the book was written, is still intense, has learned to verbalize her feeling instead of overreacting, occasionally has difficulty with sudden changes in her routine, but is now "charming, outgoing and happy."

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RADIATION ONCOLOGY

By Stewart M. Jackson, MD. 249 pp, illustrated. St. Louis, Warren Green Publishers, 1985. $37.50 (hardcover)

Dr Jackson's book is divided into three parts. The first part has a fascinating section dealing with the history and early development of radiotherapy, as well as a glossary of many terms used in radiation oncology. In addition it has chapters dealing with the assessment of cancer patients prior to radiotherapy, some decision trees in radiotherapy, and a radiotherapy compendium wherein he discusses the treatment of common cancers by radiotherapy in general terms. These chapters are somewhat skimpy for the practicing oncologist.

The second part of the text deals with the technical aspects of radiotherapy. It is profusely illustrated, with many practical examples, and should be especially valuable for technologists and dosimetrists in training. The third section entitled "Past Results and Future Prospects" deals predominantly with the methodology for evaluating end-results in oncology, and with strategies for the prevention and early detection of cancer. These are issues not unique to radiation oncology, of course, but in most larger books on oncology these important issues often get lost to the novice reader. In this text they are made to stand out.

This book has something for everyone, but should prove the most valuable for persons starting out in oncology, such as medical students, nurses, social workers, and especially radiation therapy technologists. It is well written and illustrated, has good quality printing and paper, and is of a very manageable size.

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DRG. SURVIVAL MANUAL FOR THE CLINICAL LAB

Edited by Robert J. Fitzgibbon and Bernard E. Statland, MD. 264 pp, illustrated. Oradell, NJ, Medical Economics Co., 1985. $19.95 (softcover)

This book is a collection of 33 articles updated and reprinted from *Medical Laboratory Observer* grouped within seven sections. A basic premise of this collection is that the impact of cost containment has compelled an examination of the utilization of clinical laboratory services and the cost effectiveness of those services and productivity. Survival in the DRG-created regulatory and marketplace environment is a major goal for readers of this book.

The initial articles deal with learning how to live with the DRG system. Additionally, there are discussions on the risks to laboratories, the challenges fac-

ing them, and their changing directions and roles.

The second section highlights alternatives to hospital inpatient services stimulated by the surge in competition to reduce the length of hospital stays. Ambulatory care for surgery, emergency needs, renal dialysis, alcoholism, and group practices are identified as some of the alternatives to inpatient care. Aftercare services to shorten hospital stay include skilled nursing homes, home health care, hospices, and geriatric outpatient and day care.

In this cost containment marketplace, the increasing clout of the Health Maintenance Organizations (HMOs), Independent Practice Associations (IPAs), and primary care networks is directly linked to the ability to contain the cost of health care. Obviously, the use of clinical laboratory services within all of these competitive alternatives is a major consideration of this section.

Control of laboratory utilization is covered in the third section. Critical issues discussed here involve the true need for laboratory tests, strategies to curb test abuse, and reasons why physicians order specific tests.

In the section on productivity and laboratories, attention is directed to cutting staff, reducing supply costs, and increasing output. In addition, one study identifies factors that lower productivity such as stat abuse (64%) and inefficient test ordering patterns (58%). Measures to increase productivity are also listed along with the pros and cons of buying, leasing, or renting equipment. With an emphasis on cost containment, the least and most profitable laboratory tests are identified for administrative examination.

Another section deals with the new roles for computers in clinical laboratory services. Like a popular rock song, there is talk about TRAC, TRAP, and TRIM—Test Request Audit Control, Test Request Alert Program, and Test Request Intervener and Modifier. It is evident that microcomputers will play a substantial part in containing clinical laboratory costs. However, with the technological advancements occurring daily there is no need for further details.

Section six contains articles concerning nonhospital laboratories. This is a critical issue since the DRG system constrains laboratory services on an inpatient basis relative to the bundling or unbundling determinations. Among the nonhospital sites are group practice laboratories, HMO-type laboratories, and reference laboratories.

The final section focuses on strategies to meet the DRG challenge. In this section the editors concentrate on price strategies, outpatient opportunities, use of cluster laboratory services, and the lessons learned from experiences in New Jersey laboratories. Furthermore, there is a fiscal survival plan with hints for greater laboratory efficiency as well as a review of laboratory tested survival tactics.

In summary, this book is tersely written and contains useful information for those concerned with the fate of clinical laboratories. The articles are short and go directly to the point with relevant data. The book is recommended for those who are not regular readers of *Medical Laboratory Observer* and who are concerned with the impact of DRGs on laboratory services.

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PROTEINURIA

Edited by Morrell M. Avram, MD. 232 pp, illustrated. New York, Plenum Publishing Co, 1985. $35.00 (hardcover)

This book, edited by Morrell M. Avram, MD, and contributed to by himself and a group of 34 distinguished authors, consists of 17 chapters arranged in four sections: mechanisms, clinical expressions, pathophysiologic consequences and management, and expectant or aggressive management of proteinuria. The text, prefaced by Dr Avram and epilogued by Dr R. J. Glassock, smoothly spans through 232 pages that contain a variety of tables, graphs, figures, and a few renal histopathologic and ultrastructural micrographs. Intermezzi, also penned by Dr Avram, attempts to dovetail the four major sections alluded to above.

The study of proteinuria is basically the study of nephrology. Thus it may seem from the outset that the book's title is a bit ostentatious and perhaps misleading. However, this is not the case. The scientific stature of the principal and senior authors is incontestable and following their tradition of excellence, they have put together an outstandingly clear work on some new aspects of the study of proteinuria. Nonetheless, this is not a comprehensive textbook on the subject, particularly regarding the many clinical implications of proteinuria.

As the editor indicates in his preface, "this book represents an assembly of manuscripts on proteinuria" and in this reviewer's mind it "conveys the excitement and the enthusiasm of the authors" to the readers for new knowledge, discoveries, and interpretations of the significance of proteinuria. Its style, organization, and authoritativeness have resulted in an easy-to-read, useful, and enjoyable book that constitutes a significant addition to the medical literature. It is this reviewer's opinion that the chapters by Drs Brenner, Dworkin, Robinson, Baldwin, Glassock, and Porush—and particularly the one by Dr B. D. Myers, without demeaning the value of the others—are outstanding examples of thorough and informative work in which theoretical and applied knowledge clarify complicated aspects of research in proteinuria. In addition they have concurrently generated momentum and stimulus for further research by formulating numerous questions stemming from their main line of research. This is the book's major value. Since it presents concise in-depth "state of the art" research on proteinuria, it should be considered essential reading for the nephrologist.

The book compares well with other publications in this field and I believe that the objective stated by Dr Avram when compiling this work has been amply achieved.

RODRIGO URIZAR, MD
Albany Medical Center
Albany, NY 12208

Fibrocystic disease does not always lead to breast cancer

"Fibrocystic disease" may no longer be an acceptable diagnosis, and may in fact jeopardize the health insurance of the 50 to 80% of American women who have the condition.

According to a special report published in the March issue of *Archives of Pathology and Laboratory Medicine* (1986; 110:171–173), most fibrocystic conditions do not represent precancerous breast disease. The report was the result of a meeting convened to discuss fibrocystic conditions. "This meeting was a result of a series of events that began with complaints made by women throughout the country. They individually contacted the American Cancer Society because of frustration and consternation after being told that continuation of their health insurance was in jeopardy or that their premiums would be rated higher because of a diagnosis of fibrocystic disease," the report states.

The meeting was convened by the College of American Pathologists and funded by the American Cancer Society. Participants included pathologists, oncologists, surgeons, and gynecologists.

The results of the meeting concluded that the diagnoses of "fibrocystic condition" or "fibrocystic changes" are preferable to the less specific diagnosis of "fibrocystic disease." The meeting participants also recommended that if a diagnosis is used at all, it should include component elements.

The report then lists and assigns relative risks to more than one dozen specific diagnoses. Among conditions with no increased relative risk for invasive breast cancer are adenosis, apocrine metaplasia, macro or micro cysts, duct ectasia, fibroadenoma, fibrosis, mild hyperplasia, mastitis, periductal mastitis, and squamous metaplasia.

Those diagnoses with a slightly increased risk for invasive breast cancer of one and one half to two times that of comparable women who have had no breast biopsy include hyperplasia, moderate or florid, solid or papillary; and papilloma with fibrovascular core.

Diagnoses with a moderately increased risk, up to five times that of women who have had no breast biopsy include atypical hyperplasia (borderline lesion), either ductal or lobular.

Federal guidelines for chemotherapeutic drugs

Federal guidelines for the safe use of cancer-fighting drugs are now available to pharmacists, physicians, nurses, and other health care workers who use the drugs.

The guidelines, developed by the federal Occupational Safety and Health Administration (OSHA), alert health care workers to the dangers of antineoplastic (or cytoxic) drugs frequently used in chemotherapy, which are often carcinogenic.

"Current practices in the preparation, storage, administration and disposal of drugs used in chemotherapy to treat cancer may expose pharmacists, nurses, physicians and other health care workers to high environmental levels of the same drugs," Acting Assistant Secretary of Labor Patrick R. Tyson, head of OSHA, said in a press release.

The guidelines stress the importance of proper handling in the preparation and administration of the drugs, storage, waste disposal, and handling spills. Also included in the guidelines are points on preparation and education of employees handling the drugs, appropriate use of personal protective equipment, and work practices.

The drugs are believed to have dangerous effects on humans, including reproductive impairment, organ and chromosome aberrations, birth defects, and death of tissue.

The guidelines have been sent to all major health care facilities, including general medical, surgical, and specialty hospitals (excepting psychiatric hospitals). Copies of the guidelines have also been distributed to all OSHA field offices, and to states that operate their own OSHA programs. (New York operates such a program, but only for state and local government employees.) A copy of the guidelines may be obtained by contacting state or federal OSHA offices.

California Medical Association reaffirms position on clinical ecology

The California Medical Association's scientific board has reaffirmed a 1981 position that clinical ecology does not constitute a valid description of medicine as recently reported in the *Western Journal of Medicine* (1986; 144: 239–245.)

Clinical ecologists maintain that a variety of physical and psychological ailments may be caused in susceptible individuals by continuous exposure to certain foods and environmental chemicals and inhalants. Continuous low-level exposure may reduce a sensitive individual's initial severe reaction to a particular substance, but the reaction continues to manifest itself in persistent, low-grade problems that are often misdiagnosed, clinical ecologists say. The main methods of treatment employed for these conditions are "avoidance or elimination of stressors in the diet or the environment, rotation diets, optimal dose intradermal treatment, neutralization treatment and an ecologically sound workplace and home." (*WJM* 1986; 144: 240.)

The CMA's scientific board first reviewed the practice of clinical ecology in 1981. However, as a result of requests from clinical ecologists for another opportunity to present evidence justifying their diagnostic and treatment methods, the CMA's scientific board appointed a task

force to perform another critical appraisal of clinical ecology. The task force set up criteria for the evaluation of literature on causation, prognosis, diagnostic tests, and therapy. A hearing was also held, at which presenters gave testimonials and information on additional data.

The task force found that its collected data contained a great deal of descriptions of basic hypotheses of clinical ecology, individual experience reports, and anecdotes; however, it contained few published studies proving or disproving clinical ecology hypotheses. The task force's four conclusions were: "There is no convincing evidence that supports the hypotheses on which clinical ecology is based; clinical ecologists have not identified specific, recognizable diseases caused by exposure to low level environmental stressors; methods to diagnose and treat such undefined conditions have not been shown to be effective; and the practice of clinical ecology can be considered experimental only when its practitioners adhere to scientifically sound research protocols and inform their patients about the experimental nature of their practice." (*WJM* 1986; 144: 239.)

NEWS BRIEFS are compiled and written by Sandra Cirincione.

ASSOCIATED MEDICAL SCHOOLS OF NEW YORK REQUEST FOR ANATOMICAL DONATIONS

The Associated Medical Schools of New York has received a gratifying response from people of various ages and different areas of the country to its efforts to inform the public about the immense value of anatomical donations in the education of future physicians and the discovery of new medical techniques.

Donating one's body permits medical students to gain the comprehensive understanding of human anatomy that is indispensable to a physician. In addition, anatomical donations have enabled researchers to develop new surgical techniques and gain further understanding of diseases such as cancer, diabetes, and heart disease.

The need for such donations is particularly great in the greater New York area because of the high concentration of medical and other health professions schools. Those interested in learning how a donation can be made may write to the Associated Medical Schools of New York, Bellevue Hospital Center, First Ave and 27th St, New York, NY 10016, or call (212) 686-5540.

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Achille A. Baldassarri, MD, Bayville. Died December 31, 1985; age 64. He was a 1950 graduate of New York University College of Medicine. Dr. Baldassarri was a member of the American Occupational Medical Association, the Aerospace Medical Association, the Nassau County Medical Society and the Medical Society of the State of New York.

Benjamin Beck, MD, Westbury. Died January 5, 1986; age 74. Dr Beck was a 1941 Licentiate of the Royal College of Physicians of Edinburgh. He was a Diplomate of the American Board of Family Physicians and a member of the American Geriatrics Society, the Nassau County Medical Society and the Medical Society of the State of New York.

Luke Berardi, MD, Mount Vernon. Died November 19, 1985; age 73. He was a 1938 graduate of St. Louis University School of Medicine. Dr Berardi was a member of the Medical Society of the County of Westchester and the Medical Society of the State of New York.

William Basil Bilecky, MD, New York. Died December 29, 1985; age 67. He was a 1943 graduate of Marquette University School of Medicine, Milwaukee. Dr Bilecky was a member of the New York County Medical Society and the Medical Society of the State of New York.

William Alexander Briscoe, MD, New York. Died December 22, 1985; age 67. He was a 1942 graduate of the University of Oxford School of Medicine. Dr Briscoe was a Fellow of the American College of Physicians and a member of the Academy of Medicine, the American Society for Clinical Investigation, the American Thoracic Society, the New York County Medical Society and the Medical Society of the State of New York.

Cemil Emirgil, MD, Valhalla. Died October 22, 1985; age 66. Dr Emirgil was a 1944 graduate of the Istanbul Universitesi Tip Fakültesi. Dr Emirgil was a member of the American Thoracic Society, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Joshua Epstein, MD, Union City, NJ. Died December 17, 1985; age 82. Dr Epstein was a 1926 graduate of Tufts University School of Medicine, Boston. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Samuel Johnson Fairstein, MD, Mount Vernon. Died January 22, 1986; age 77. He was a 1935 graduate of Dalhousie University Faculty of Medicine, Halifax. Dr Fairstein was a Fellow of the American College of Anesthesiologists and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Frances Gould Finder, MD, Santa Cruz, California. Died December 29, 1985; age 79. Dr Finder was a 1931 graduate of Medizinische Fakultät der Universität, Wien. Dr Finder was a member of the American Psychiatric Association, the New York County Medical Society and the Medical Society of the State of New York.

Serge Arthur Giraldi, MD, New Rochelle. Died December 8, 1985; age 64. He was a 1954 graduate of Università Degli Studi di Bologna, Facoltà di Medicina e Chirurgia. Dr Giraldi was a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the American Geriatrics Society, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Ephraim Julius Goldman, MD, Syracuse. Died December 15, 1985; age 87. Dr Goldman was a 1923 graduate of McGill University Faculty of Medicine, Montreal. He was a member of the Onondaga County Medical Society and the Medical Society of the State of New York.

Rose Merriman Lenahan, MD, Buffalo. Died January 12, 1986; age 84. She was a 1937 graduate of the University of Buffalo School of Medicine. Dr Lenahan was a Fellow of the American College of Anesthesiologists, a Diplomate of the American Board of Anesthesiology and a member of the Academy of Medicine, the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc., the Medical Society of the County of Erie and the Medical Society of the State of New York.

Philip Lieblich, MD, Brooklyn. Died October 27, 1985; age 75. He was a 1939 graduate of Uniwersytet Jana Kazimierza Wydzial Lekarski, Lwow-Lemberg. Dr Lieblich was a Fellow of the American Academy of Family Physicians and a member of the New York Cardiological Society, the American Geriatrics Society, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Edwin R. Linwood, MD, Bellmore. Died January 21, 1986; age 81. He was a 1930 graduate of Columbia University College of Physicians and Surgeons, New York. Dr Linwood was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Orthopedic Surgery. His memberships included the American Academy of Orthopaedic Surgeons, the Nassau County Medical Society and the Medical Society of the State of New York.

Benjamin Palmer Malerba, MD, Long

Island City. Died January 24, 1986; age 83. Dr Malerba was a 1928 graduate of George Washington University School of Medicine. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Marshall M. Menzies, MD, West Islip. Died January 7, 1986; age 83. Dr Menzies was a 1929 graduate of Temple University School of Medicine, Philadelphia. He was a Diplomate of the American Board of Otolaryngology, a member of the Medical Society of the County of Oneida and the Medical Society of the State of New York.

Lester Lynn Merritts, MD, Mineola. Died October 3, 1985; age 44. He was a 1965 graduate of Università Degli Studi di Bologna, Facoltà di Medicina e Chirurgia. Dr Merritts was a Fellow of the American College of Cardiology and a Diplomate of the American Board of Internal Medicine. His memberships included the New York State Society of Internal Medicine, the Nassau County Medical Society and the Medical Society of the State of New York.

Saul D. Miller, MD, New York. Died December 18, 1985; age 79. Dr Miller was a 1938 graduate of Université de Lausanne Faculté de Médecine. He was a member of the American Psychiatric Association, the New York County Medical Society and the Medical Society of the State of New York.

Leroy Henry Pedersen, MD, Flushing. Died January 1, 1986; age 64. Dr Pedersen was a 1946 graduate of the State University of New York Downstate Medical Center. He was a Diplomate of the American Board of Internal Medicine and a member of the Queens County Medical Society and the Medical Society of the State of New York.

Philip Harvey Prose, MD, Brooklyn. Died January 1, 1986; age 70. He was a 1941 graduate of Université de Lausanne Faculté de Médecine. Dr Prose was a Diplomate of the American Board of Dermatology, Inc., and the American Board of Pathology. His memberships included the New York Pathological Society, the American Association of Pathologists and Bacteriologists, the Society for Investigative Dermatology, the Medical Society of the County of Kings and the Medical Society of the State of New York.

Paul Melbourne Read, MD, Adams. Died December 30, 1985; age 79. He was a 1931 graduate of the University of Toronto Faculty of Medicine. Dr Read was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Urology. His memberships included the American Urological Association, the Medical Society of the County of Jefferson and the Medical Society of the State of New York.

Aaron Schual, MD, Northport. Died January 6, 1986; age 74. Dr Schual was a 1937 graduate of Università Degli Studi di Padova, Facoltà di Medicina e Chirurgia. He was a member of the American Psychiatric Association, the Suffolk County Medical Society and the Medical Society of the State of New York.

Edward E. Sheldon, MD, New York. Died December 22, 1985; age 73. He was a 1936 graduate of Uniwersytet Warszawski Akademie Medyczna, Warsawa. Dr Sheldon was a Diplomate of the American Board of Radiology and a member of the Radiological Society of New York State, the New York County Medical Society and the Medical Society of the State of New York.

Arden Henry Snyder, MD, Port Charlotte, Florida. Died December 1, 1985; age 71. Dr Snyder was a 1943 graduate of the University of Buffalo School of Medicine. He was a member of the Medical Society of the County of Monroe and the Medical Society of the State of New York.

Rocco A. V. Spano, MD, Buffalo. Died December 20, 1985; age 94. He was a 1919 graduate of Università di Napoli Facoltà di Medicina e Chirurgia. Dr Spano was a member of the Academy of Medicine, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Helen Gertrude Walker, MD, Williamsville. Died December 8, 1985; age 92. She was a 1928 graduate of the University of Buffalo School of Medicine. Dr Walker was a Fellow of the American College of Physicians and the American College of Chest Physicians. Her memberships included the New York State Society of Internal Medicine, the American Medical Women's Association, the American Thoracic Society, the Medical Society of the County of Erie and the Medical Society of the State of New York.

Florence E. Warner, MD, Binghamton. Died November 25, 1985; age 83. Dr Warner was a 1927 graduate of Cornell University Medical College. She was a member of the Broome County Medical Society and the Medical Society of the State of New York.

Daniel A. Wilcox, MD, Katonah. Died January 22, 1986; age 81. He was a 1932 graduate of Columbia University College of Physicians and Surgeons. Dr Wilcox was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Alvin Davis Yasuna, MD, Southbury, Connecticut. Died October 2, 1985; age 77. Dr Yasuna was a 1933 graduate of New York University College of Medicine. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Stanley Sanford Zipser, MD, New York. Died December 3, 1985; age 74. He was a 1936 graduate of the State University of New York Downstate Medical Center. Dr Zipser was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the New York County Medical Society and the Medical Society of the State of New York.

Guidelines for authors

Originality

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089-1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

Preparation

An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), an abbreviated title of no greater than 40 spaces for use as a running foot, and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

Categories

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

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For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

Figures

The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

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References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

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Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83:925-927.
2. McGuigan JE. Peptic ulcer. In: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD, eds. *Harrison's Principles of Internal Medicine*. New York, McGraw-Hill, 1983, pp 1697-1712.

Review

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

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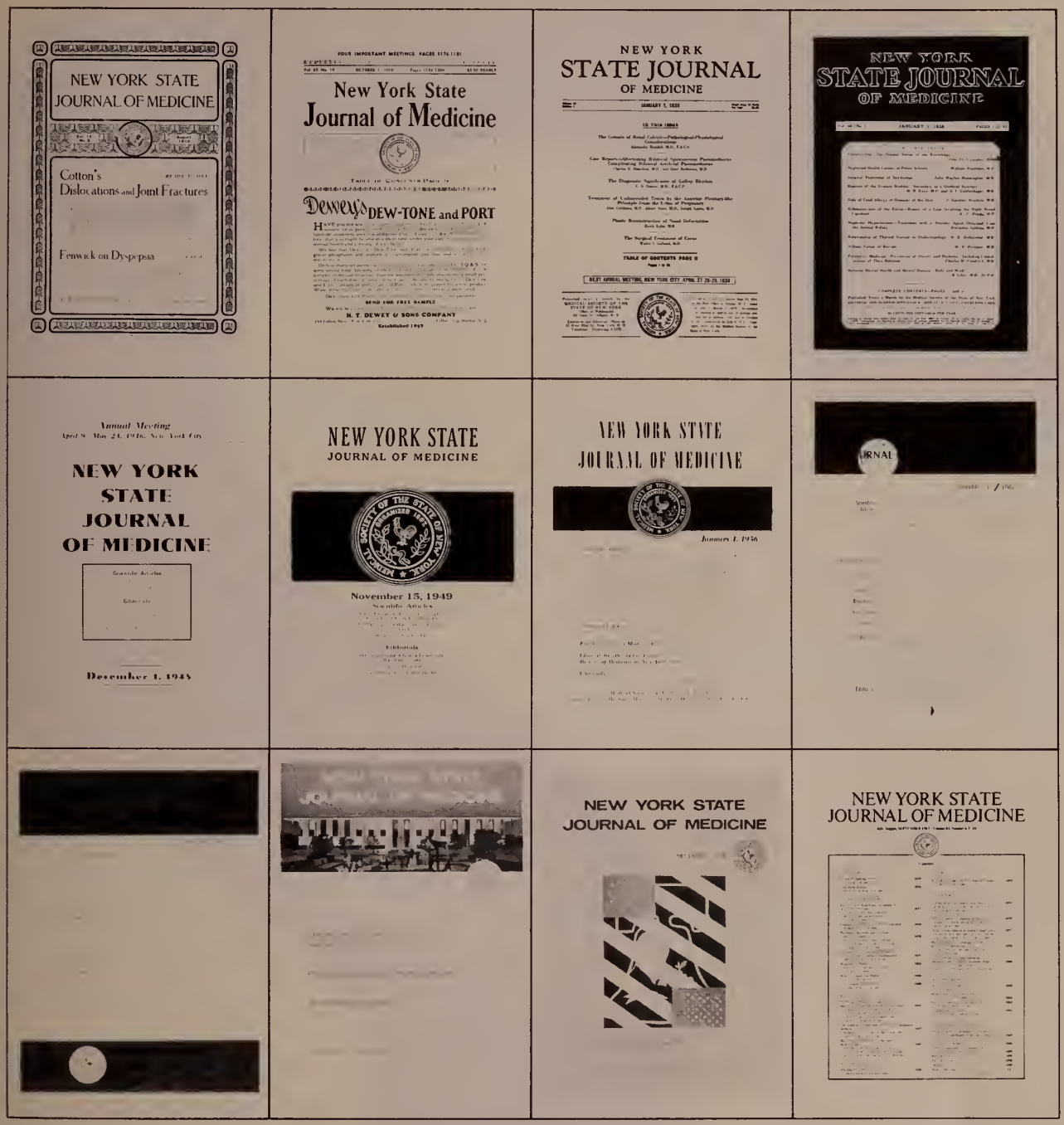

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May 6. **Pediatric Urology: Obstructive Uropathies.** *May 13.* **Sports Medicine: Cardiovascular Aspects.** *May 20.* **Pediatric Ophthalmology.** Info: Arthur J. Schwager, MD, Director, Continuing Pediatric Medical Education, Huntington Hospital, Park Ave, Huntington, NY 11743. Tel: (516) 427-0530.

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May 8. **Monthly Medical Conference: The Leukemia's.** 1 Cat 1 Credit. *May 23.* **Continuing Medical Education Lecture: Breast Cancer.** 1 Cat 1 Credit. Info: Jodi Horton, Director, Public Relations and Development, St Joseph's Medical Center, 127 South Broadway, Yonkers, NY 10701. Tel: (914) 965-6700, ext. 535.

May 14. **Hematology Day.** Info: Toni Calabrese Boelsen, Coordinator, White Plains Hospital Medical Center, White Plains, NY 10601. Tel: (914) 681-1118.

ALBANY

May 1–3. **Geriatric Medicine and Rehabilitation.** Americana Inn. Info: Barbara G. Post, Program Coordinator, Sunnyview Hospital and Rehabilitation Center, 1270 Belmont Ave, Schenectady, NY 12308. Tel: (518) 382-4500.

MONROE

May 3–4. **Current Aspects of Surgical Pathology.** 8 Cat 1 Credits. Grossinger's. Info: Nathan S. Taylor, MD, Department of Pathology, Rochester General Hospital, 1425 Portland Ave, Rochester, NY 14621. Tel: (716) 338-4121.

WARREN

May 19–21. **38th Annual Scientific Assembly of the New York State Academy of Family Physicians.** Sagamore Inn on Lake George, Bolton Landing. Info: John J. Falencki, MD, Chairman, 1986 Committee Meeting, New York State Academy of Family Physicians, 30 West State St, Colonial Pl, Binghamton, NY 13901-2332. Tel: (607) 722-7205.

ONONDAGA

May 30–31. **Application of the CO_2 Laser in Otolaryngology.** Sheraton University Inn. Info: Program Coordinator, Office of Continuing Education, Upstate Medical Center, State University of New York, 750 East Adams St, Syracuse, NY 13210. Tel: (315) 473-4606.

AROUND THE NATION

CALIFORNIA

May 7–10. **American Association for Cancer Research.** Los Angeles Convention Center. Info: McGettigan's Corporate Planning Services, 1609 Walnut St, Philadelphia, PA 19103. Tel: (800) 523-4614.

May 15–17. **19th Annual Advances and Controversies for Clinical Pediatrics.** 16 Cat 1 Credits. Mark Hopkins Hotel. *May 22–23.* **Current Issues in Anatomic Pathology: 1986.** 12 Cat 1 Credits. Union Square Holiday Inn. Info: Extended Programs in Medical Education, University of California, San Francisco, CA 94143. Tel: (415) 666-4251.

(*Continued on p 18A*)

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May 27–31. **15th Annual Society of Critical Care Medicine Educational and Scientific Symposium.** 40 Cat 1 Credits. Info: Tracy Schultz, Program Coordinator, Society of Critical Care Medicine, 223 East Imperial Hwy, Suite 110, Fullerton, CA 92635. Tel: (714) 870-5243.

KENTUCKY

May 18–23. **17th Family Medicine Review.** 50 Cat 1 Credits. Hyatt Regency Hotel, Lexington. Info: University of Kentucky College of Medicine, Office of Continuing Education, 132 COM Office Building, Lexington, KY 40536-0086. Tel: (606) 233-5161.

MASSACHUSETTS

May 1–3. **Topics in Internal Medicine.** 16 Cat 1 Credits. Dunfey's Parker House. Info: Department of Education, Lahey Clinic Foundation, Inc, 41 Mall Rd, Burlington, MA 01803. Tel: (617) 273-8807.

May 5–8. **Pulmonary Medicine.** Copley Plaza Hotel. 24 Cat 1 Credits. Info: Harvard Medical School, Department of Continuing Education, Boston, MA 02115. Tel: (617) 732-1525.

May 12–16. **22nd National Conference on Breast Cancer.** 31 Cat 1 Credits. Marriott Copley Place. Info: American College of Radiology, Breast Cancer Conference, 1891 Preston White Dr, Reston, VA 22091. Tel: (703) 648-8900.

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ENGLAND

May 10–14. **Fourth Annual London Spring Seminar in Diagnostic Imaging.** 20 Cat 1 Credits. Info: Medical Seminars International: Spring Seminar, 21015 Roscoe Blvd, Suite 222, Canoga Park, CA 91304. Tel: (818) 340-0580, ext. 280.

ISRAEL

May 24–28. **The International Symposium on Eating Disorders in Adolescents and Young Adults.** Info: Secretariat, The International Symposium on Eating Disorders in Adolescents and Young Adults, P.O. Box 394, Tel-Aviv, 61003, Israel.

ITALY

May 2–4. **Third International Conference on Myopia.** Rome. Info: Sylvia N. Rachlin, Myopia International Research Foundation, Inc, 1265 Broadway, Room 608, New York, NY 10001. Tel: (212) 684-2777.

SCOTLAND

May 31–June 10. **Plastic and Reconstructive Surgery in Scotland.** 16 Cat 1 Credits. Info: Francine Leinhardt, Program Coordinator, Manhattan Eye, Ear and Throat Hospital, 210 East 64th St, New York, NY 10021.

MISCELLANEOUS

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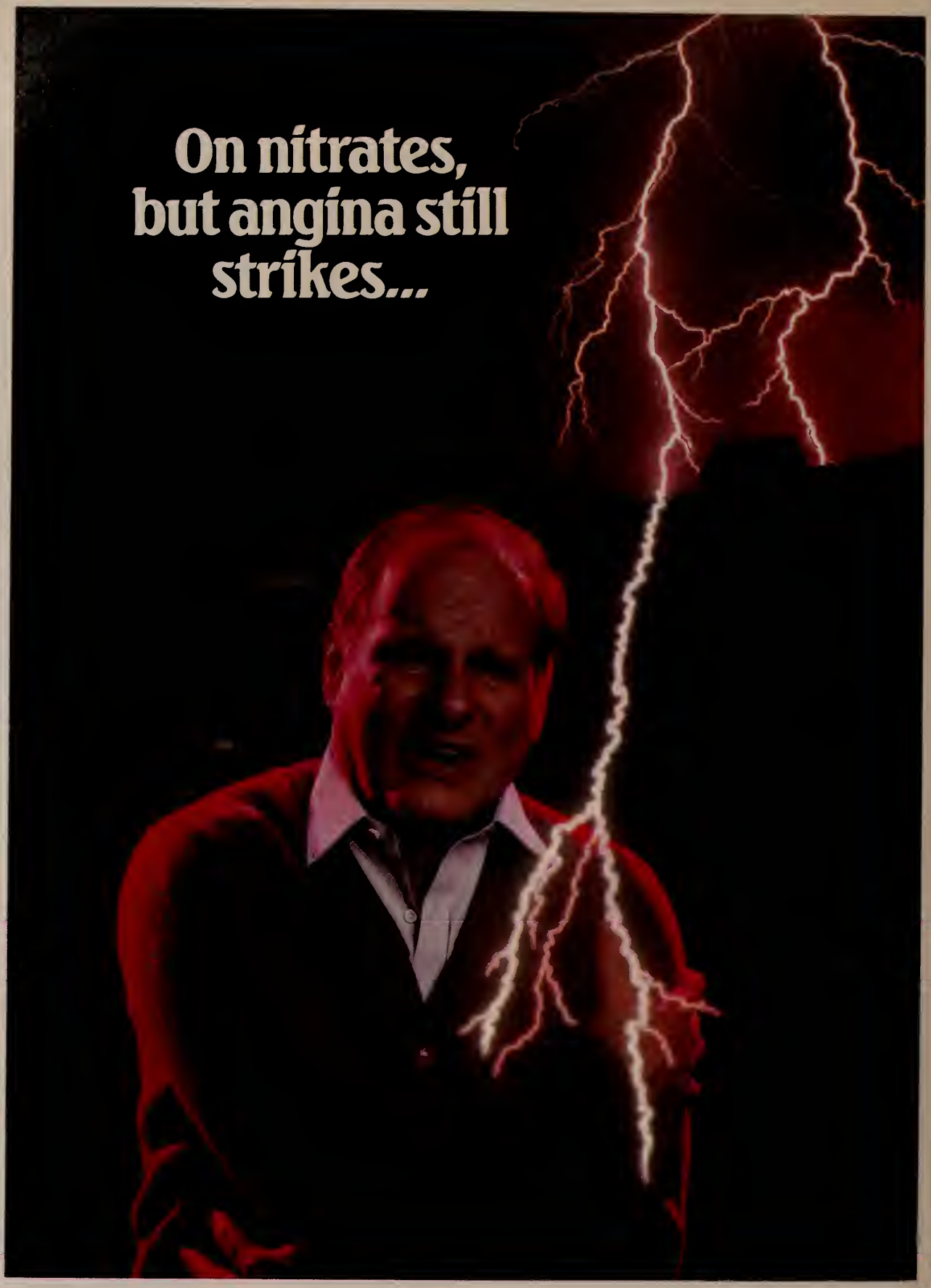
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(See *Warnings.*) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecomastia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984 2385

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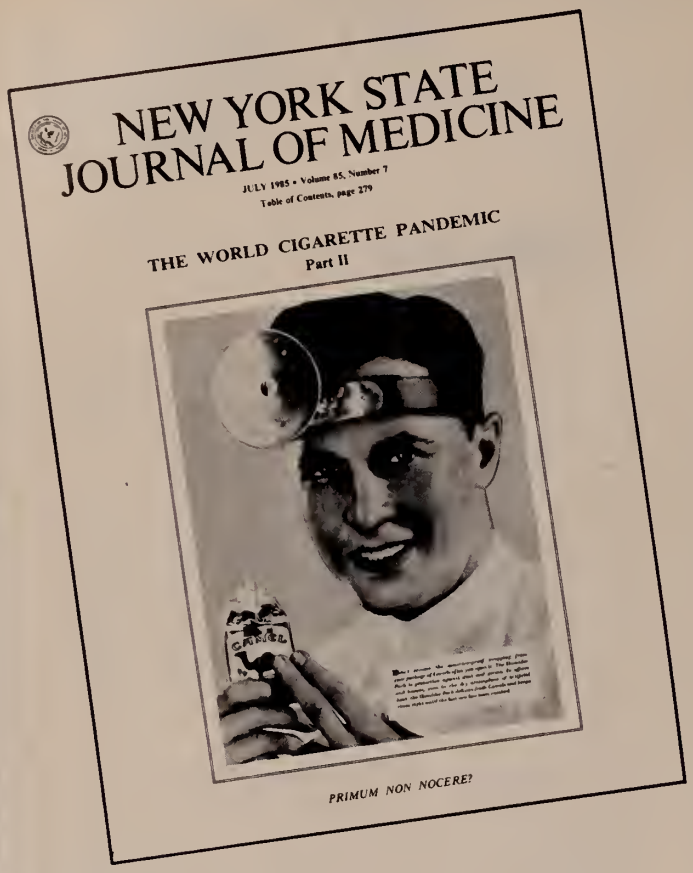

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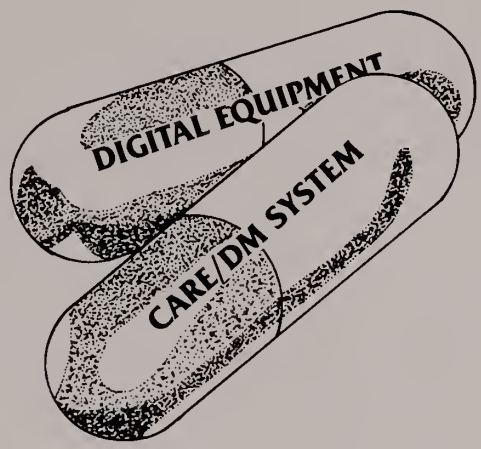

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APRIL 1986 • Volume 86, Number 4A

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Prepared by the Medical Society of the State of New York (MSSNY) Committee on Health Care Delivery Systems, and the Division of Medical Services, who gratefully acknowledge the California Medical Association's (CMA) source material as primary references in the development of these guidelines.

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A Word of Caution

No organization can collectively bargain for physicians who are not employees. Decisions on whether to negotiate with a service plan or other entity, whether or not to sign the negotiated rate of compensation, and all other decisions about the provision of service are up to the individual physician. It is recommended that any agreement or contract under pressure or without sufficient information to make an informed decision should not be signed; the final decision is up to the individual.

Introduction

In view of the rapid change in the delivery of health care and the proliferation of health care delivery systems, the medical profession is being confronted with increasing competitive challenges. Consequently, many physicians may be considering contractual arrangements with third party entities to further their medical practices.

While "contracting" may not be a new concept, the current cost containment thrust from public, governmental, and health insuring sources in the midst of a surplus physician population has created significant interest in arrangements that produce a fundamental change in the traditional patient-physician relationship. A fundamental change characterizing these new contracting arrangements is the insertion of the previous third party payor into the traditional patient role, even to the point that the payor influences the type of medical care to be rendered. In essence, the physician/patient relationship is modified to include the health care delivery business entity.

A physician presented with a contract for services faces a complex decision since risk-sharing and quality medical care considerations may have a significant impact on a physician's practice. Physicians are therefore reminded that a contract is a legal document that imposes binding responsibilities on the parties concerned. Typically, the business entity's involvement reaches beyond mere reimbursement for services to include authorization for treatment, utilization review, restricted referrals, increased liability exposure, and many other issues that may impact on a physician's medical decision-making. However, physician responsibility to a patient is not altered by a contract, and professional liability should be a major concern to physicians considering the execution of a contract.

The MSSNY guidelines are designed to help physicians deal prudently with contractual arrangements they may be considering. Since this is a dynamic and continually changing area, these guidelines should not be considered the final word on this issue.

New York State Law

Article 44 of the New York State Public Health Law identifies Health Maintenance Organizations (HMOs) as "any person, natural or corporate, or any groups of such persons who enter into an arrangement, agreement, or plan, or any combination of arrangements or plans which propose to provide or offer, or which do provide or offer, a comprehensive health service plan."

In New York State no person or groups of persons may operate a health maintenance organization, or issue a contract to an enrollee for membership in a comprehensive health services plan without first obtaining a certificate of authority from the Commissioner of Health.

At this time no Preferred Provider Organization (PPO) legislation exists in New York State. However, the MSSNY will continue to monitor the attitudes of pertinent state agencies relative to various health care delivery systems, including PPOs.

For-profit medical referral services are prohibited by New York law. Section 4500 of the Public Health Law states, "medical referral services organized as profit making enterprises within this state have been found to be engaged in the practice of medicine, have been sharing fees received for referrals with doctors and hospitals to whom patients are referred, have been otherwise compensating doctors and hospitals for accepting patients referred to them, have been giving medical advice by telephone to persons seeking referrals and have been advertising their services, all in violation of the standards of ethics and public policy applicable to the practice of medicine . . . ."

Section 4501 of the Public Health Law provides that no person, firm, partnership, association, or corporation may engage in for-profit only business or service that in whole or in part includes the referral or recommendation of persons to a physician, hospital, or health-related facility.

The MSSNY has reviewed some contracting arrangements that, in part, require the physician to pay a fee in order to be on a referral list. It is important that a physician offered such a contract ascertain whether the contract may be regarded as an illegal medical referral service.

Antitrust Considerations

Section I of the Sherman Antitrust Act of 1890 states "Every contract, combination in the form of trust or otherwise, or conspiracy in restraint of trade of commerce . . . is declared to be illegal . . . ." The US Antitrust law was enacted to protect competition and thereby preserve the free market system. Theoretically, competitive markets are maintained by the Antitrust law's prohibition of monopoly, price fixing, boycotts, and other restraints of free trade.

The US Supreme Court decided in 1975 that the learned professions—medicine among them—are subject to federal antitrust laws. Still, since 1975 there has been very little case law developed in this area. However, in June of 1982, the Supreme Court, in the case of Arizona *v* Maricopa County Medical Society, found Sherman Act violations when medical society foundations, by agreement of their member physicians,

The Position of the Medical Society of the State of New York (MSSNY) on Health Care Delivery Systems

No single pattern of health care delivery is necessarily suited to all patients or to all physicians

The traditional fee-for-service, HMO, HMO-IPA, and PPO concepts are valid and acceptable health care delivery systems

There must be available multiple delivery mechanisms among which both the patient and the physician can truly exercise the right of free choice of how they will receive and disburse quality medical care

Employers should contribute equitable amounts for each employee's health benefit plan, regardless of the plan selected

Fair market competition among all systems of health care delivery shall continue to be MSSNY policy (similar to AMA policy) with the potential growth of health care delivery systems being determined not by governmental intercession or entrepreneurial considerations, but by the number of people who prefer this mode of delivery

established the maximum fees physicians would claim in payment for specified health services. The Supreme Court found such maximum fee agreements per se* violations of Section I. Similar agreements to set minimum fees are also per se violations of the Act.

The Court concluded that a per se violation is found where a price restraint tends to provide the same economic rewards to all practitioners regardless of their skill, experience, training, or willingness to employ innovative and difficult procedures in individual cases. Such a policy, the Court reasoned, is a restraint and discourages entry into the market and may deter new developments by individual entrepreneurs.

Although the Supreme Court admitted its limited experience with the health care industry, "The Sherman Act, so far as price-fixing agreements are concerned, establishes one uniform rule applicable to all industries alike." The Court views the anticompetitive potential in all price-fixing agreements as being per se violations of the Sherman Act despite the existence or procompetitive justifications for some price-fixing agreements.

The clear lesson to be learned from Maricopa is that "Any combination that tampers with price structures is engaged in unlawful activity. Even though the members of the price-fixing group were in no position to control the market, to the extent that they raised, lowered or stabilized prices, they would be directly interfering with the free play of the market forces." Thus, the conduct of physicians cannot include explicit or implicit agreements to tamper with or establish price structures.

Physicians should not attempt to effect a boycott of any contracting entity. And, if physicians band together as a group in an attempt to "fix" fees, the US Supreme Court considers that "price fixing" in violation of antitrust laws. That point is clear from the Maricopa decision. *Physicians do have a right to exchange information and to express an opinion about a particular contract or contracting entity.* That right is protected by the First Amendment, as long as the information or opinion sticks carefully to the truth. But the decision to sign or not to sign a contract is in the hands of individual physicians. Groups of physicians—including organized medicine as represented by the MSSNY—have no right to tell a physician that he or she should or should not sign a contract.

Violations of Antitrust Laws

The following are some activities that may be in violation of antitrust laws.

- Communications and/or concerted activity regarding prices and exchanges of price or cost information from which an inference may be drawn that competing providers are affecting price.
- Communications and/or concerted activity from which it may be inferred that competing providers agree not to compete as to a particular service, geographic area, or patient market.
- Concerted activity by competing providers to refuse to deal with a particular third party payor.
- Communications and/or concerted activity between one provider group and a third party payor that affect the compensation of another provider group.
- The formation of entities for the sole purpose of jointly negotiating fees with third party payors.
- Control of a third party payor by providers whose compensation is determined by the third party payor.

Entities Offering the Contract

Prudent business practices mandate that physicians be aware of the legitimacy and fiscal soundness of business entities offering contracts. Before analyzing any contract and before entering into any contract, a physician should determine the propriety and financial track record of the business entity. It should be noted that many health care delivery systems take different forms and names. No particular nomenclature is absolute and it would not be practical to attempt to address every entity seeking to contract with physicians. However, the following are a few terms that have become generic.

Health Maintenance Organization (HMO). An organization, for profit or nonprofit, that accepts responsibility for the provision and delivery of a predetermined set of comprehensive health services for a voluntarily enrolled group at a prepaid and fixed payment.

Individual Practice Association (IPA). Generally a partnership, association, corporation, or other legal entity that delivers, or arranges for the delivery of health services. Usually, the entity accepts a capitation rate and a degree of risk.

Preferred Provider Organization (PPO). A group of health care providers (physicians and hospitals) that contracts with employers, insurance companies, or third party administrators to deliver medical services on a fee-for-service basis (usually discounted) to a specific group of beneficiaries.

Questions to Ask About a Contract†

While no satisfactory definition of the term "contract" exists, a contract is generally regarded as a binding agreement between two or more persons or parties. However, every contract involves at least one promise that has legal consequences. Physicians must never forget that a contract is a legally enforceable agreement. Therefore, the utmost care and thought must be given to understand the legal obligations created by a contract. The following questions will assist physicians in identifying specific obligations created in a contract relationship. Note that there is no correct set of answers. Each question is designed to create an awareness of potential issues to be considered when analyzing a contract proposal.

One should never assume that one understands all terms, clauses, and phrases. One should ask questions as to what specific words and language are intended by the drafter to mean. No list of questions is complete.

I. Questions to ask about the business entity.

1. Is the business entity clearly identified?
2. Who owns and controls the business entity?
3. Who sits on the Board of Directors of the business entity?
4. Who are the principal officers of the business entity?
5. Does the business entity need to be licensed to conduct its business within the state?
6. Does the business entity transact business within the state under other names?
7. Can the business entity provide copies of certified and/or audited balance sheets and profit and loss

* The per se rule is an antitrust law standard governing activities that are *automatic* violations of the antitrust laws. The per se standard is applied to activities that are considered so inherently anticompetitive that there is no justification for them.

† Adapted from the *Physicians Contracting Handbook*, San Francisco, CA, California Medical Association, 1985, pp 43–52, with permission.

statements for the past five years?

8. Is the business entity willing to disclose a list of contract physicians who may be used as references?
9. Is the business entity willing to disclose a list of employer groups and/or employee groups who are presently receiving health benefits as a result of a contractual relationship with the business entity?
10. Within what counties in the state does the business entity intend to contract with physicians?
11. Has the business entity provided copies of any and all contracts offered to physicians within the state?
12. Is the business entity obligated to carry professional liability insurance?
13. If the business entity carries professional liability insurance, does the professional liability insurance extend coverage to physicians under contract?
14. Does the business entity require contracting physicians to carry professional liability insurance?
15. Does the business entity require that the contracted physician name the business entity as an insured on the physician's liability insurance policy?
16. Has the business entity's insurance carrier confirmed that coverage is in force?
17. Does the business entity subcontract for utilization review, peer review, and/or related activities?
18. Does the business entity's professional liability insurance extend coverage to the activities of subcontractors?
19. Does the business entity require by contract that subcontractors maintain professional liability insurance?
20. Does the contract allow the business entity to assign the contract to other business entities?
21. In what other states is the business entity offering contracts to physicians?
22. Is the business entity offering contracts to hospitals within the state?
23. *Has the business entity submitted its plans and systems to the US Department of Justice or the Federal Trade Commission for review of compliance with federal antitrust statutes and trade regulations, and made any review or opinion letter available?*
24. Is the business entity presently a party to any professional liability litigation and/or dispute?
25. Is the business entity presently under investigation by the US Department of Justice or Federal Trade Commission?

II. Questions to ask about the contract.

26. Are all the parties to the contract clearly identified by name?
27. Does the contract contain any blank spaces?
28. Under what circumstances can the physician terminate the contract?
29. How much advance notice is required for the physician to terminate the contract?
30. Does the contract attempt to incorporate by reference into the contract documents that the physician has not seen or reviewed?
31. Does the contract require that the physician hold harmless and indemnify the business entity and/or any intermediary from any liability arising from the physician's rendering of professional services?
32. Is the contract an exclusive contract, prohibiting the physician from contracting with competing business entities?
33. Does the contract restrict the physician's traditional referral patterns by requiring that referrals be made only to contracting physicians and to contracting institutional providers?
34. Is the physician familiar with the referral resources available under the contract?
35. Does the contract require that the physician maintain a specified dollar amount of professional liability insurance?
36. Does the contract contain an open-ended utilization review clause requiring the physician to follow unspecified review policies?
37. Does the contract allow for the contract to be unilaterally amended by the business entity without the agreement or assent of the physician?
38. Do all provisions in the contract relating to medical records comport with state law?
39. Does the contract require that a physician participate in peer review activities for the business entity?
40. Does peer review immunity granted to physicians under state law extend to physicians who perform review for a business entity rather than a medical society or hospital staff?
41. If a contract specifies that review functions will be performed by non-physicians, does the contract describe the professional qualifications required to be a review coordinator?
42. Does the contract require that each physician member of a partnership or a professional corporation execute the agreement?
43. Has the contract been reviewed by the physician's professional liability insurance company to determine whether the contract affects the physician's existing insurance coverage?
44. Does a contractual requirement that the physician submit to arbitration any contractual dispute and/or professional liability dispute affect the physician's existing professional liability insurance coverage?
45. To what extent does a contractual agreement to arbitrate disputes preclude the physician from pursuing a course of action through the courts?
46. Does the contract automatically roll over from year to year without the physician indicating a willingness to continue the contractual relationship?
47. What impact does the termination of the contract have upon the physician/patient relationship?
48. Does the contract require that the physician keep proprietary information confidential?
49. Does the contract contain any contractual restrictions upon the physician's ability to practice medicine consistent with prevailing standards of care?
50. Does the contract make vague reference to "practice cost effective medical and surgical care" and/or "innovative cost containment techniques"?
51. Has a representative of the business entity made any oral or written representation concerning the physician's contractual relationship that is not embodied in the written contract?
52. Does the contract require that the physician notify

patients of the physician's decision to terminate the contractual relationship?

53. If the contract contains a grievance procedure, does the contract fully explain all the steps and requirements of such a grievance procedure?
54. If the contract provides for a grievance committee, are members of the grievance committee appointed or elected?
55. Does the contract require the physician to pay application fees or annual dues?
56. Does the contract limit referrals to "contract" laboratory and/or x-ray facilities?
57. Does the contract limit the physician's independent and professional judgment regarding the involvement of an assistant surgeon, anesthesiologist, etc?
58. Does the contract limit the time for the submission of claims?
59. Does the contract provide for payment of claims to the physician within a specified time limit?
60. Does the contract provide for a penalty if payment to the physician is delayed?
61. Does the contract specifically provide that the agreement will be governed by the law of another state?
62. Does the contract provide some readily available method of identifying patients under the contractual relationship?
63. Does the contract require that the physician call and verify patient identification prior to each consultation?
64. Is the business entity bound by its verification of eligibility of a contract patient?
65. Does the contract clearly define and specify noncovered services?
66. Does the contract provide that the patient is liable for payment of noncovered services?
67. Does the contract allow the physician's name to be used on brochures, other advertising, radio and/or television?
68. Has the physician carefully reviewed any and all documents referenced in the contract?
69. Does the contract require written and/or other prior authorization before the commencement of specified procedures?
70. Does the contract list the specific procedures that require prior authorization?
71. Does the contract provide for the physician to receive prior authorization in a timely and reasonable manner?
72. Does the contract require the physician to modify existing office procedures and/or billing systems?
73. Does the contract require that the physician's status as a "contract" physician is conditioned upon the physician maintaining medical staff privileges at one or more contracting hospitals?
74. Does the contract obligate the physician to provide any services after the contract is terminated?
75. Does the contract allow for the fee schedule to be unilaterally changed without prior notice to the physician and/or without the prior assent of the physician?
76. Does the contract limit the number of patients the physician may (or must) serve over the course of a year?
77. Does the contract require the physician to be available on a 24-hour basis?
78. Does the contract require that a "contract" physician arrange for another "contract" physician to cover during absences and vacations?
79. Does the contract refer to unspecified medical policies?
80. Does any party to the contract have the right to unilaterally change medical policies?
81. Does the contract provide an opportunity to examine the experience and qualifications of "contract" referral physicians?
82. Does the contract require the physician to accept all patients referred under the contractual relationship?
83. Does the contract limit the right of a physician to contract with any other third party?
84. Does the contract permit termination if the contractor becomes insolvent?
85. Does the contract place cost concerns ahead of quality concerns?
86. Is the contract an arrangement of potentially competing physicians who have joined to fix prices, divide markets, or boycott others?
87. Does the contract specifically exclude from coverage services rendered by any recognized specialty?
88. Does the contract provide for a "gatekeeper" approach to the delivery of health care?

III. Questions to ask about professional liability.

89. Does the contract contain broadly worded indemnification clauses that attempt to shift risks from the business entity to the physician?
90. Does the physician's existing professional liability insurance cover any assumed contractual liability under the terms and conditions of the contract?
91. Does the contract directly or indirectly interfere with the physician's exercise of good medical judgment?
92. What is the name of the professional liability insurance company that insures the business entity?
93. Is the business entity's professional liability insurance "claims-made" or "occurrence" coverage?
94. Has the business entity allowed the physician an opportunity to request and review the business entity's professional liability insurance policy?
95. What is the extent of a "contract" physician's liability if the business entity is found liable on a theory of corporate negligence?
96. Does the physician's liability insurance protect the physician from liability on charges of violation of antitrust laws?
97. Will the business entity provide a list of attorneys specializing in medical malpractice defense work who are customarily and regularly retained by the business entity to handle professional liability claims?
98. If the contract requires the physician to perform review functions outside the medical staff and/or medical society setting, how will the business entity establish standards, criteria, and norms that will be used in this review process?
99. Does the business entity assume liability for utilization review decisions that are contrary to the attending physician's medical judgment?

100. Does the business entity screen applicant physicians in such a manner as to limit or reduce the possibility of corporate negligence?
101. Does the business entity carry sufficient insurance to cover business entity administrative mistakes or deficiencies that deny or limit care?

The Effect of Contracting on Referral Patterns

Contracts being offered to physicians may contain expressed and/or implied restrictions on referral patterns. For example, the following language from a physician contract restricts established referral patterns: "Provider shall recommend to patients in order to promote cost control that they use other participating providers in the service area in which the patient resides and agrees not to refer patients to non-participating providers without prior authorization of (business entity)."

Because such restrictions are risky in that they limit a physician's referral possibilities, physicians are advised to satisfy themselves as to the adequacy of referral resources before execution of such a contract. While physicians have a legal responsibility to refer patients to appropriate specialists, the business entity may not have a sufficient variety of specialists under contract, thereby restricting access to needed medical care and possibly resulting in adverse consequences. However, physicians should also recognize that a physician who refers a patient to a noncontracting provider may be liable for that provider's charges to the patient, if the patient does not accept the financial consequences of such a referral.

Furthermore, it should be recognized that physicians providing temporary and/or on-call coverage for contracting physicians may not have contracts. In that instance, when the on-call physician bills the patient he or she is paid less than the contracting physician would receive. Unless the on-call physician is willing to accept this payment, the patient—who believes that there is no "balance bill" under an arrangement with a business entity—will get a bill for the balance. The patient may blame his own physician for arranging on-call coverage by a noncontracting physician (fee disputes may foment professional liability litigation).

Professional Liability Exposure

It should initially be noted that a person may be legally and financially responsible for actions that are not up to established standards of care. Professionals with special skills are held to a special standard of care. Thus, physicians have a duty to their patients to act as a reasonable physician would act, given similar circumstances. If the physician is a specialist, he or she is held to the standard of the reasonable specialist in the same field. The physician not only has an ethical duty to provide the best care he or she can, but also has a legal duty to provide at least the same quality of care as a reasonable physician would have provided under similar circumstances.

The standard of care is a fluid concept, designed to reflect current local practice, technology, and teaching. The practice of defensive medicine has influenced the physician's standard of care. The practice of defensive medicine leads to the use of tests and procedures that may minimize statistically slight risks, and make diagnosis more precise. This practice may produce a very high standard. Meeting this high standard of care may be very expensive, but may not necessarily be cost-effective.

Consequently, all parties involved in contractual arrangements between insurers and physicians should understand that these arrangements for health care may present new risks of liability. Everyone involved in contracting should be aware that the risk of a suit may increase in this new environment. The gravest danger arises from the apparent contractual restrictions upon quality care and treatment.

Arrangements with contracting entities may significantly differ from traditional insurance coverage. One feature is agreement between the physician or other provider and the insurer as to the amount to be paid for specific services. From the professional liability standpoint, other features of these arrangements could be even more significant since benefit contracts may financially impact on patients who are treated by noncontracting providers, and many procedures cannot be performed on an inpatient basis, except with prior authorization.

Despite the impact of these conditions or restrictions on the physician's ability to treat a patient in his or her usual manner, applicable standards of medical practice are the same, regardless of the insuring arrangement. As previously stated, the risk of suit increases in this environment. If the physician refuses to adhere to a business entity's limitations on medical treatment, the physician could be personally liable for breach of contract. However, if a physician adheres to the contract rather than the established standard of care, and the patient is adversely impacted, then the physician may be liable for any adverse patient occurrence. The fact that a physician was following contractual limitations or procedures is no defense since the contract itself does not provide protection for the physician. The established standard of care cannot be altered by a contract.

Therefore, a contracting entity's refusal to authorize or pay for care that ought to be rendered, in good medical practice, does not, of itself, excuse the physician who fails to render or offer such care. Physicians should not assume that the responsibility for the exercise of good medical judgment has passed to the carrier; that responsibility remains with the physician. The carrier may have an independent and equal responsibility in exercising good medical judgment, but a carrier's medical policy may not excuse a physician who accepts the carrier's judgment.

Since contracts may include significant lists of services that cannot be provided without prior authorization, physicians should determine whether the business entity's authorization scheme is compatible with good medical practice before signing a contract. Circumstances may arise where carriers will not authorize or may otherwise obstruct the provision of needed care. When this occurs, it is imperative that physicians document the circumstances. If an authorization for treatment is denied contrary to the physician's best medical judgment, the decision should be challenged. Equally important, physicians should explain the problem to the patient, describe the care that the physician believes is needed, and, insofar as possible, assist the patient, either in resolving the dispute with the carrier, or in finding an alternative source of care.

Physicians who blindly accept carrier restrictions or decisions they consider to be erroneous may be liable for the consequences. The carrier may also be sued, but this is small comfort to the physician, even if greater liability is ultimately

assessed against the carrier.

Even physicians who acquaint their patients with these problems and exhaust all available "administrative remedies" —without avail on the patient's behalf—may be sued. Some patients will believe that the physician did not do enough to provide the needed care. Even if the patient does not sue the physician, the carrier itself may try to lay blame on the treating physician. Administrative mistakes or deficiencies that deny or limit care, affecting the outcome, place carriers and those involved in plan administration at great risk. These entities may be liable to the patient on theories of negligence, misrepresentation, breach of contract, and "bad faith," with possible punitive damages being sought by the patient. These cases may be so threatening to contracting entities that they may attempt to find reasons for physician culpability. Thus, the threat to the physician may not only be the threat of suit by a patient, but the threat of challenge by a contracting entity.

One of the assumptions being made by those who favor contracting is that less care will be rendered if no payment or reduced payment is available, thereby decreasing the cost of care. Whatever financial benefits this prospect might have, it is possible that some necessary care will not be rendered. It is believed that courts may not require patients to bear the burden in these situations, even though they willingly chose this form of coverage (courts reputedly make every effort to protect patients).

Even where there is no personal injury, physicians may be sued by patients who suffer economic loss because of the physician's alleged failure to work within an arrangement. Physicians who refer patients to noncontracting physicians or who admit patients to noncontracting hospitals, will have to be extremely careful that the patient understands and approves of any financial consequences. Generally, the consequence may be additional unreimbursed expense to the patient. Where such referrals are necessitated by the carrier's failure to arrange for adequate resources, thorough documentation is strongly recommended. These patients may blame their own physicians for arranging coverage by noncontracting physicians or hospitals, and contend breach of contractual responsibility, thus possibly fomenting professional liability litigation.

It is important that the business community and insurers who are interested in contracting arrangements recognize that such arrangements, by their very nature and purpose, carry with them additional exposure to suit. It is even more important that physicians recognize this risk. In many cases, patients will not discriminate between various potential defendants. Even defendants themselves may bring others into such litigation. Those entering into these new arrangements should be aware of these risks and consult knowledgeable attorneys before agreeing to contracting terms.

In addition, physicians should not presume that all risks they assume in carrying out the provisions of contractual arrangements are protected under their liability insurance coverages. For example, the execution of a "hold harmless" clause could render a physician "bare" as to assumed contractual liability, since professional liability insurance policies may exclude from coverage any liability assumed under contract. Under these circumstances, a physician could be required to expend personal finances in defense of a contracting business entity. A hold harmless clause in a contract may read as follows: "The Physician shall be responsible for the quality of care rendered to the participants and shall hold harmless, indemnify and defend the Business Entity, its administrators, officers, directors, and trustees from any litigation costs, claims, judgments, liability and damages resulting from the medical, surgical and/or dental care rendered to the participant under this contract, including any legal damages, costs of adjustments or investigation, attorney's fees or any other costs." However, the language could be as simple as the following: "The Physician agrees to hold Business Entity harmless as to any liability arising from this contract."

Physicians are, therefore, urged to consult with their insurers to determine the extent and limitations of their liability protection under these circumstances.

Noteworthy Issues That May Appear in Physician Contracts[‡]

It must be kept in mind that a contract proposed by a health care delivery system does not always protect and promote the best interests of physicians. Entrepreneurs, lawyers, accountants, and business entity executives who draft contracts for these systems should not be underestimated in their efforts to shift liability to physicians, restricting the manner in which physicians practice medicine, and exercise control over physicians through various contractual provisions. Physicians may, therefore, wish to seek the inclusion of language in contracts that will protect their interests.

While the following sample language may not appear in current contracts offered in New York State, physicians should be aware that such language may appear in future proposals.

Open-Ended Utilization Review

Sample Language.

- "Participating physician shall participate in a Utilization Review Program approved by (Business Entity)."
- "The Physician agrees to cooperate fully with innovative approaches to cost containment."
- "In-patient services are subject to authorization of the Review Coordinator."
- "(Business Entity), or its designated organization or agent, shall conduct retrospective review to determine whether out-patient services were medically necessary."

Problem.

- Utilization review standards not specified and set forth; may be inconsistent with physician's standard of care.
- Innovative approaches, cost containment not defined; may be inconsistent with standard of care.
- Qualifications of review personnel making medical decisions are unknown.
- Utilization review procedures and standards may directly affect outcome.

Ramifications.

- Increase in administrative burdens.
- Physician may be liable for treatment or failure to treat, which does not meet the established standard of care.
- Business entity may also be liable, but a physician who blindly accepts business entity's judgments may also be liable.
- Physician's risk of financial and professional liability is increased.

[‡] Adapted from the *Physicians Contracting Handbook*, San Francisco, CA, California Medical Association, 1985, pp 29–42, with permission.

Conclusion.

- Physicians should be informed of specific utilization review plans and procedures in order to determine whether their contractual obligations are acceptable and/or increase liability exposure.

Arbitration Clause

Sample Language.

- "Any controversy or claim arising out of or relating to this agreement shall be settled by arbitration in accordance with the rules of the American Arbitration Association, and judgment on the award rendered by the arbitrator or arbitrators may be entered in any court having jurisdiction thereof. Any party to this agreement may submit to arbitration any said controversy or claim."
- "Physician agrees to submit any dispute concerning a Utilization Review decision, unresolved by reconsideration or review, to binding arbitration. The scope of that arbitration shall be limited to a determination of whether, or to what extent, benefits specified in the applicable employee benefit group agreement were medically necessary."

Problem.

- May force most, if not all, disputes to arbitration.
- Slow process.
- Limited appeal of arbitration awards.
- Does not involve review by "peers."

Ramifications.

- May preclude litigation entirely.
- The parties must pay arbitration expenses and fees.
- Legal advice still necessary, and each party is liable for its own legal fees and perhaps the other party's fees.

Conclusion.

- Physicians should not view arbitration as inexpensive and easy. Resort to litigation may be severely limited.

Termination

Sample Language.

- "The term of this Agreement shall be for a period of one (1) year, and shall thereafter be extended for successive periods of twelve (12) months, unless terminated by either party. Any party desiring to terminate the Agreement must serve notice at least sixty (60) days prior to the conclusion of the current term and will continue to be bound by its provisions until the conclusion of such term."
- "Contracting Physicians shall, at (Business Entity's) election, continue to provide Covered Physician Services to Plan Enrollees so long as any (Business Entity) contract providing for enrollment in the Plan remains in effect, which shall in no event exceed fourteen (14) months from the time such termination is effected."
- "(Business Entity) may terminate Agreement at any time for cause."

Problem.

- Physician's ability to terminate the contract may be severely restricted.
- Physician contract term may be tied to patient contract term and therefore cannot be terminated until patient contract expires.
- Business entity may have the right to terminate the contract at will, effective immediately; the physician may not have such a right.
- The contract may automatically renew without renegotiation of terms or fees.

Ramifications.

- Contract provisions, including fee schedules, may be in effect for indefinite period.
- Contractual duties may extend past "termination" date.
- Contract termination does not necessarily terminate patient-physician relationship; physician could be liable if patients are abandoned without proper medical care.

Conclusion.

- Physicians should determine how to terminate contractual obligations, if termination is possible.

Confidentiality Requirements

Sample Language.

- "Physician may, from time to time, receive information from (Business Entity) that (Business Entity) designates in writing as confidential. Physician agrees that such information shall be kept confidential and shall not be disclosed to any person except as authorized in writing by (Business Entity)."

Problem.

- Ambiguous.
- Could be interpreted to require withholding of information from staff, colleagues, payors and/or patients.

Ramifications.

- Inadvertent disclosure of information could be breach of contract; physician could be liable for any damages.
- Failure to disclose information could be inconsistent with the physician's standard of care.

Conclusion.

- Physicians should seek clarification as to what the business entity considers confidential and exactly what the physician's obligations may be regarding the business entity's confidential documents.

Entire Agreement Clause

Sample Language.

- "Any prior agreements, promises, negotiations or representations, either oral or written, relating to the subject matter of this Agreement not expressly set forth in this Agreement are of no force or effect."
- "This Agreement contains all the terms and conditions agreed upon by the parties hereto regarding the subject matter of this Agreement."

Problem.

- Written contract may not include party's oral representations or understandings.
- A business entity's representations may differ from the contract terms.

Ramifications.

- Only printed terms of the contract may be binding.
- Oral promises, sales pitches, statements in solicitations, or other papers may not be enforceable.

Conclusion.

- Physicians should make certain that the written contract fully reflects their understanding of all obligations and rights.

Open-Ended Grievance Procedures

Sample Language.

- "(Business Entity) shall develop, adopt and implement a

grievance and appeal mechanism which provides a patient with the opportunity to file a complaint and resolve disputes regarding those professional medical services rendered by Physician."

- "Any complaint by and between any persons entitled to care under this Agreement shall be subject to the complaint procedure described in the Member's Handbook."
- "Provider agrees to comply with (Business Entity's) member grievance procedures and to abide by the decision of its Grievance Committee."

Problem.

- Grievance procedures not specified.
- Composition of committee unknown or subject to unilateral appointment by the PPO or business entity.

Ramifications.

- Blind agreement to follow unknown procedures may constitute waiver of impartial hearing.
- Grievance procedure may limit physician's right to litigate.
- Grievance committee may not be neutral.

Conclusion.

- Physicians should obtain and review grievance procedures prior to executing a contract.

Restricted Referral

Sample Language.

- "Contracting Physician shall arrange for the provision of Covered Physician Services, on a non-emergency basis, only by referral to other Contracting Physicians, and all such referrals shall be coordinated through the Plan Medical Director."
- "The Doctor agrees that when a referral to a specialist or hospitalization is required, and whenever reasonably possible, to make such a referral to a specialist or hospital under contract with the (Business Entity). Referrals to a specialist or hospitalization may be subject to prior authorization, except in an emergency situation."
- "Physician agrees to refer all Members, when not treatable by Physician, only to physicians under contract with (Business Entity) unless (Business Entity) does not have a needed specialist."

Problem.

- Disruption of established referral patterns.
- Lack of familiarity with the qualifications of other contracting physicians or contracting hospital(s).
- Lack of privileges at contracting hospital(s).
- No apparent standards for authorization of referral/hospitalization.
- Business entity may not have contracted with adequate number or variety of specialists or hospitals.

Ramifications.

- Physician may be blamed for consequences of referral to "contract" physician whose qualifications are unknown or inadequate.
- Physician may be liable to patient for economic loss due to physician's failure or refusal to refer patient to a "contract" hospital or physician.

Conclusion.

- Physicians must satisfy themselves as to the adequacy of referral resources prior to signing a contract. If referrals to noncontracting hospitals and physicians are in a patient's best medical interests, physicians should ensure that the patients understand and accept the financial consequences.

Professional Liability Insurance Requirements

Sample Language.

- "Physician, at his/her sole cost and expense, shall provide and maintain such policies of general liability and professional liability insurance and other insurance as shall be necessary to insure Physician and his/her personnel and agents against any claim or claims for damages arising by reason of personal injuries or death occasioned directly or indirectly in connection with the performance of any service provided hereunder, the use of any property and facilities provided by Physician, or his/her personnel in connection with this Agreement. The amount and extent of such coverage shall be subject to the approval of (Business Entity). To the extent feasible, Physician shall use his/her best efforts to have (Business Entity) named as an additional insured on any such insurance policies. Documentary evidence of the above insurance policies shall be provided to (Business Entity) upon request. Physician shall notify (Business Entity) thirty (30) days prior to any change in such insurance coverage."
- "Provider shall carry Professional Liability Insurance in the minimum amount of one million dollars for any one incident and three million dollars in the annual aggregate, and wherever possible, shall name Business Entity as an additional insured."
- "Providers shall carry professional malpractice and general comprehensive insurance in amounts consistent with industry standards and in full compliance with all applicable Payor contracts."

Problem.

- Dollar amount of professional liability insurance may not be specified.
- Business entity may unilaterally change the required dollar amount of professional liability insurance.
- The contract may require that the physician purchase higher limits of professional liability insurance.
- The physician's professional liability insurer may not allow the business entity to be named as an additional insured on the physician's policy.

Ramifications.

- Business entity may attempt to shift liability to the physician's professional liability insurer.

Conclusion.

- Prior to signing the contract, each physician should ascertain the dollar amount of insurance required under the contract and, in consultation with his or her insurer, determine if the contract affects the physician's existing insurance coverage.

Medical Records and Confidentiality

Sample Language.

- "Physician shall provide PPO, Participating Physicians, and any duly designated third party with reasonable access to medical records of Participating Patients maintained by Physician during the term of this Agreement, and thereafter for a period in conformance with state law after the termination of this Agreement, and at any time thereafter that such access is required in connection with a Participating Patient's medical care. PPO shall be enti-

tled to obtain copies of Participating Patient's medical records at Physician's expense."

- "To the extent permitted by law, Professional Program Participants shall cooperate and communicate freely with other Professional Program Participants and with other persons providing health care services to Beneficiaries and shall integrate records of Beneficiaries with the records of other Professional Program Participants or other person providing health care services to any such Beneficiary."

Problem.

- Broad language authorizing disclosure of medical records.
- Physician may absorb expense of reproducing voluminous medical records.

Ramifications.

- Physician may be liable for damages caused by unwarranted disclosure of a patient's medical records.
- Contractual requirements do not supersede existing state laws protecting confidentiality of medical records.

Conclusion.

- Physicians should seek professional advice and should not rely on contractual language for protection from liability for improper disclosure of medical records.

Peer Review

Sample Language.

- "Physician agrees to comply with the peer review system established by (Business Entity). Parties acknowledge and agree that review programs and procedures may be changed from time to time at (Business Entity's) sole discretion."
- "Physician agrees to abide by the peer review process of Corporation, and to follow peer review rules, regulations and protocols, and to participate in the peer review process of Corporation, if requested by the Chairman of the Peer Review Committee."

Problem.

- Peer review may involve participation of the physician and/or application of the peer review process to the physician.
- No apparent standards and procedures for peer review.
- Business entity has power to unilaterally change peer review standards and procedures.

Ramifications.

- Reviewing physician could be sued for defamation or interference with practice.
- Statutes that normally grant conditional immunity from suit to physicians conducting peer review, typically for medical society or hospital medical staff review activities, may not apply to private contracting review.
- If immunity does apply, it will depend on the facts in each case.
- Peer review conducted solely for cost-containment purposes may impact upon the provision of patient care, exposing physicians to increased administrative expense, bureaucratic processes, and professional liability.

Conclusion.

- Physicians should weigh potential disadvantages before agreeing to a contract, which imposes "peer review" controls, and particularly before agreeing to be a participant in the application of those controls.

Assignable Contract

Sample Language.

- "Provider will not assign his/her/its rights, duties or obligations under this Agreement either in whole or in part without the written consent of (Business Entity); however, that an assignment by Business Entity to any of its affiliates or subsidiaries shall be permissible at any time."
- "(Business Entity) shall have the right to assign this Agreement to any other person, firm or corporation, provided that the assignee shall expressly assume and agree to perform all obligations of (Business Entity) under this Agreement."

Problem.

- Business entity may at any time assign physician's obligations under the contract to another business entity without the physician's prior approval.
- Substituted party may lack adequate financial resources and/or lack administrative capabilities.

Ramifications.

- To assign a contract is to substitute one of the original contracting parties with a different party.
- Physician may end up performing services for an entirely different business entity (the assignee). For example, if a physician signed a contract with the ABC PPO and the ABC PPO "assigned" its interest in the contract to the XYZ PPO, the physician may be required to perform contractual obligations for the XYZ PPO.

Conclusion.

- Physician should be aware that an assignable contract could obligate the physician to provide services to a different group of patients or payor than originally planned.

Amendment/Modification

Sample Language.

- "(Business Entity) may modify this Agreement by providing notice to Physician of any proposed amendment. The failure of the Physician to object to any such proposed amendment within ten (10) days of receipt of notice shall constitute acceptance. All other amendments or modifications to this Agreement shall be mutually agreed to in writing by (Business Entity) and Physician."
- "Provider agrees that the provisions of this Agreement, the rules and regulations and the traditional rules and regulations to be adopted from time to time by Administrator, are subject to amendment by Administrator from time to time upon sixty (60) days' written notice to Provider and that Provider shall thereafter be bound by the provisions as so amended, provided, however, that if Provider delivers to administrator at any time during the first thirty (30) days of such sixty (60) day period written notice of Provider's election to terminate this Agreement shall immediately so terminate."

Problem.

- Broad power vested in the business entity to unilaterally change the contract.
- Physician may not possess similar right to unilaterally change the contract.

Ramifications.

- Physician may be obligated to comply with any change.
- Any part of the contract—fee schedule, utilization standards, etc—may be subject to unilateral change.
- Physician may be required to either accept unilateral changes or terminate entire contract.

Conclusion.

- Broad unilateral modification clauses may make a contract completely open ended and therefore subject to unilateral determinations of a business entity.

Billing and Payment

Sample Language.

- "As part of their contracts with PPO, Payors are agreeing to either pay, or advise Participating Physicians of the reasons for nonpayment, within thirty (30) days of receipt of the original bill in such form and containing such information as required by Payor."
- "(Business Entity) shall pay Physician within thirty (30) days of receipt of billings which are accurate, complete and otherwise in accordance with Section 6.8."
- "Such sum shall be payable by (Business Entity) to contractor on or before the 60th day following receipt of billing including all necessary surgical, consultation, medical and billing reports."

Problem.

- Actual information required for billing is not specified.
- Payment to physician may be conditioned on receipt of "required information."

Ramifications.

- Compliance with contractual billing requirements may necessitate changes in physician's current billing system, at the physician's expense.
- The absence of a guaranteed turnaround time on claims may affect physician's cash flow.
- Physicians may be without legal remedy to require payment for services within a reasonable time.
- PPO or business entity may unilaterally determine when payment will be made to the physician.

Conclusion.

- A physician should request specific, detailed contractually required billing information and formats prior to signing the contract, in order to determine what effect compliance may have on physician's overhead and income.

Blank Spaces

Sample Language.

- "This Agreement shall become effective on . . . , 198 . . . , and shall continue in effect until . . . , 198 . . . ."
- "Contractor shall be responsible for, and have complete control of, the rendering of the following services to Enrollees: . . . Such services shall be rendered at the following locations: . . . Such services shall be rendered during the following hours: . . . ."
- "Compensation based on multiplying the 1974 RVS Unit Value for a performed medical consultation by $ . . . and for a performed surgical procedure by $ . . . ."

Problem.

- Significant contract terms omitted.

Ramifications.

- Possible presumption that physician agreed to terms as later completed by PPO or business entity.
- May give PPO or business entity the opportunity to unilaterally determine contract terms.

Conclusion.

- Physicians should refrain from signing contracts containing blank spaces.

Summary

The MSSNY urges that quality and cost effective medical care continue to be the primary concern of physicians practicing in the cost containment environment of health care delivery settings, thus sustaining their role as patient health care advocates; and advises physicians contemplating contractual arrangements with health care delivery systems to:

- ascertain whether the utilization review and quality control activities of the prospective organization are conducted by a cross-section of physician participants predicated on community health care standards; with technical input provided as required;
- ascertain whether the prospective organization makes provision for medical staff selection of physician representative(s) to actively participate in the system's governance, management, and fiscal operations, to ensure the appropriateness of the organization's activities, eg, medical policy, and equitable disbursement of finances to the medical staff;
- be aware that these arrangements may present new risks of non-medical and medical liability, and consult with attorneys and medical liability insurers accordingly, before signing a contract;
- be cognizant of the fact that since no organization may collectively bargain for physicians who are not employees, decisions on whether to negotiate with a service plan or other entity, or to accept the negotiated rate of compensation, and all other decisions relative to the provision of service, are up to the individual physician; consequently, any agreement or contract offered under pressure, or without sufficient information to make an informed decision, should not be signed;
- become thoroughly familiar with the terms of the agreements (including items that may be merely referenced, but not included in an agreement, eg, by-laws, medical policy, details of compensation, exclusivity arrangements, etc), before signing contracts, and should consult attorneys, appropriate consulting services, as well as the "Physicians Contracting Guidelines" promulgated by the MSSNY and disseminated to component county medical societies for this purpose.

Furthermore, a physician's first resource for assistance is generally the county medical society, which will be in the best position to know which health care delivery systems or business entities are offering contracts. The county medical society may also be able to provide referrals to experts, ie, attorneys, accountants, and/or consulting services, who are familiar with physician contracts. Physicians may wish to seek the specialized skills of legal practitioners experienced in representing physicians, especially in the antitrust and physician contracting fields. However, physicians seeking professional legal advice should also determine whether the legal practitioner has any conflicts of interest, such as representing the health care delivery system or business entity in question.

The MSSNY will continue to monitor all pertinent developments relative to health care delivery systems and provide information to its membership through the local county medical societies and through appropriate MSSNY publications.

The MSSNY Committee on Health Care Delivery Systems will endeavor to review and compare the policies of contracting entities to current MSSNY guidelines and make recommendations to the Council of the society, accordingly.

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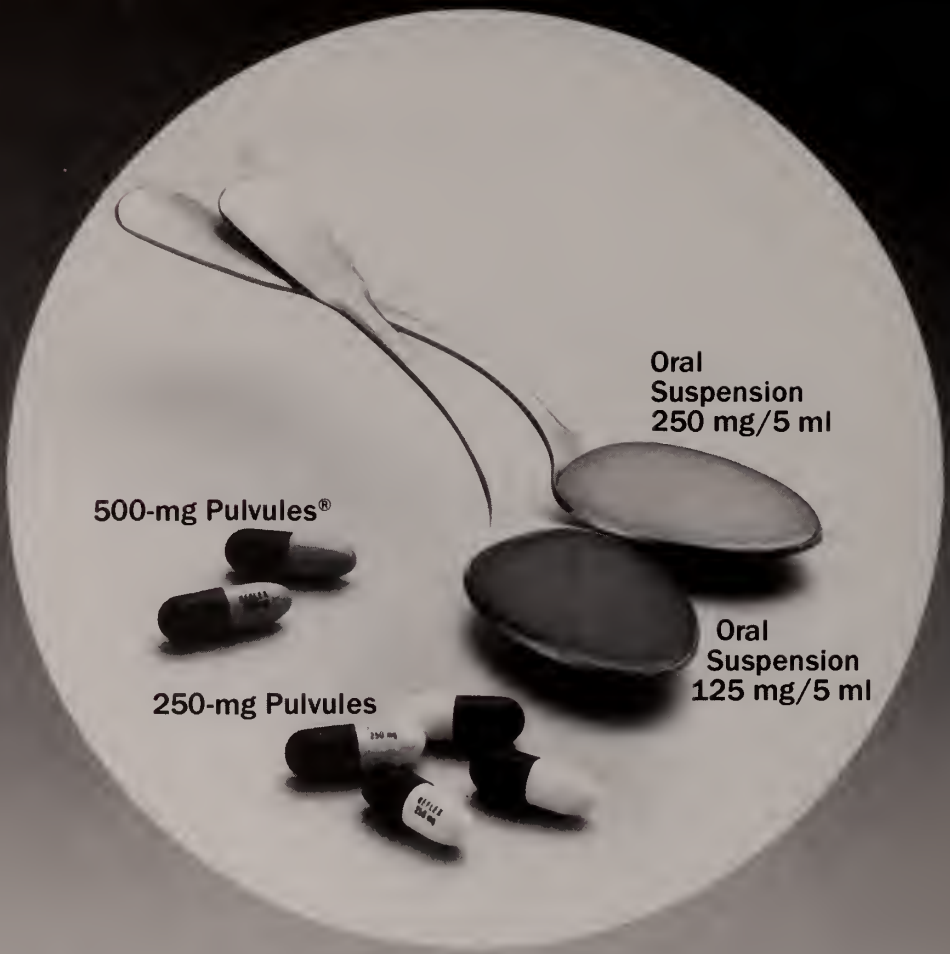

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(theophylline anhydrous) Sustained Action Tablets

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Description: THEO-DUR sustained action tablets contain anhydrous theophylline, a bronchodilator, in a sustained release formulation (with no color additives) which allows a 12-hour dosing interval for a majority of patients and a 24-hour dosing interval for selected patients.
Clinical Pharmacology: Theophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator and smooth muscle relaxant. The drug also produces other actions typical of the xanthine derivatives: coronary vasodilator, cardiac stimulant, diuretic, cerebral stimulant, and skeletal muscle stimulant. The actions of theophylline may be mediated through inhibition of phosphodiesterase and a resultant increase in intracellular cyclic AMP. Apparently, no development of tolerance occurs with chronic use of theophylline.
Indications: THEO-DUR is indicated for relief and/or prevention of symptoms of bronchial asthma and for reversible bronchospasm associated with chronic bronchitis and emphysema.
Contraindications: THEO-DUR is contraindicated in individuals who have shown hypersensitivity to theophylline or any of the tablet components.
Warnings: Excessive theophylline doses may be associated with toxicity; serum theophylline levels should be monitored to insure maximum benefit with minimum risk. Incidence of toxicity increases at serum levels greater than 20 mcg/ml. High blood levels of theophylline resulting from conventional doses are correlated with clinical manifestation of toxicity in: patients with lowered body plasma clearances, patients with liver dysfunction or chronic obstructive lung disease, and patients who are older than 55 years of age, particularly males. There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may occur in up to 50% of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity. Many patients who have higher theophylline levels exhibit tachycardia. Theophylline products may worsen pre-existing arrhythmias.
Precautions: THEO-DUR TABLETS SHOULD NOT BE CHEWED OR CRUSHED. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, in the elderly (especially males) and in neonates. In particular, great caution should be used in giving theophylline to patients with congestive heart failure. Frequently, such patients have markedly prolonged theophylline serum levels with theophylline persisting in serum for long periods following discontinuation of the drug. Use theophylline cautiously in patients with history of peptic ulcer. Theophylline may occasionally act as a local irritant to the G.I. tract although gastrointestinal symptoms are more commonly centrally mediated and associated with serum drug concentrations over 20 mcg/ml.
Individuals who are rapid metabolizers of theophylline, such as the young, smokers, and some non-smoking adults, may not be suitable candidates for once-daily dosing. These individuals will generally need to be dosed at 12 hourly or sometimes 8 hourly intervals. Such patients may exhibit symptoms of bronchospasm near the end of a dosing interval, or may have wider peak-to-trough differences than desired.
Usage in Pregnancy: Animal reproduction studies have not been conducted with theophylline. It is not known whether theophylline can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Xanthines should be given to a pregnant woman only if clearly needed.
Nursing Mothers: It has been reported that theophylline distributes readily into breast milk and may cause adverse effects in the infant. Caution must be used if prescribing xanthines to a mother who is nursing, taking into account the risk-benefit of this therapy.
Pediatric Use: Safety and effectiveness of THEO-DUR administered every 24 hours in children under 12 years of age, and every 12 hours in children under 6 years of age, have not been established.
Adverse Reactions: The most consistent adverse reactions are usually due to overdose and are:
Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, diarrhea.
Central nervous system: headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
Cardiovascular: palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, ventricular arrhythmias.
Respiratory: tachypnea.
Renal: albuminuria, increased excretion of renal tubular and red blood cells, potentiation of diuresis.
Others: rash, hyperglycemia and inappropriate ADH syndrome.
How Supplied: THEO-DUR 100 mg, 200 mg and 300 mg sustained action tablets are available in bottles of 100, 500, 1000 and 5000, and in unit dose packages of 100.
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Revised 12/83

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MEETINGS AND LECTURES

The New York State Journal of Medicine *cannot guarantee publication of meetings and lectures unless the information is submitted at least three months prior to the event.*

JUNE 1986

AROUND THE STATE

MANHATTAN

June 4. **Management of Patients with Organic Impotence: A Comprehensive Review for the Non-Surgeon.** Info: Beverley R. Baptiste, Medical Education Office, Beth Israel Medical Center, First Ave at 16th St, New York, NY 10003. Tel: (212) 420-2849.

June 5–7. **Surgical Courses in Lens Implantation.** 20 Cat 1 Credits. Info: Ruth Green, Administrator, Ophthalmological Foundation of America, 823 United Nations Pl, New York, NY 10017. Tel: (212) 986-4848.

June 6. **Total Bone Marrow Transplantation in Lymphomas and Leukemias.** *June 23.* **Medical Aspects in Quality Assurance Review.** Info: Bettye Soffer, New York State Department of Social Services, Office of Disability Determinations, 110 Williams St, New York, NY. Tel: (212) 587-3891.

June 7–8. **Fine Needle Aspiration of the Breast and Thyroid Gland.** 12 1/4 Cat 1 Credits. *June 16–20.* **Emergency Medicine 1986.** 27 1/2 Cat 1 Credits. *June 23–26.* **9th Annual Review of Selected Topics in Pediatrics.** 22 Cat 1 Credits. Info: Registration Office, NYU Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

June 9–13. **Update Your Medicine: 1986.** 42 1/2 Cat 1 Credits. Info: Update Your Medicine Coordinator, New York Hospital-Cornell Medical Center, 1300 York Ave, D-115, New York, NY 10021. Tel: (212) 472-6119.

June 14. **Otolaryngology Update: 1986.** 7 Cat 1 Credits. Info: Kristen M. Johnson, Administrator, Department of Otolaryngology, Manhattan Eye, Ear and Throat Hospital, 210 East 64th St, New York, NY 10021. Tel: (212) 838-9200, ext. 2448.

BROOKLYN

June 19. **18th Annual Ophthalmology Alumni Day of the State University-Kings County Hospital.** Info: Celeste Hinton, State University of New York, Downstate Medical Center, Box 58, 450 Clarkson Ave, Brooklyn, NY 11203.

NASSAU

June 4. **Frontiers in Cardiac Imaging: MRI.** *June 18.* **Rectal Cancer: Advances in Multidisciplinary Management.** Info: Medical Education Department, Mercy Hospital, 1000 North Village Ave, Rockville Centre, NY 11570. Tel: (516) 255-2260.

June 6. **Conference for Caregivers of Infants, Toddlers, and Their Families.** Garden City Hotel. Info: North Shore Child and Family Guidance Center, 480 Old Westbury Rd, Roslyn Heights, NY 11577. Tel: (516) 626-1971.

June 10. **Pathology as an Aid in the Diagnosis and Management of the Colon.** Info: The Community Hospital at Glen Cove, St Andrews La, Glen Cove, NY 11542. Tel: (516) 676-5000.

June 20. **Selected Topics in Neurology.** 6 Cat 1 Credits. Info: Bernard W. Berkowitz, MD, Department of Neurology, Nassau County Medical Center, 2201 Hempstead Tpke, East Meadow, NY 11554. Tel: (516) 542-3107.

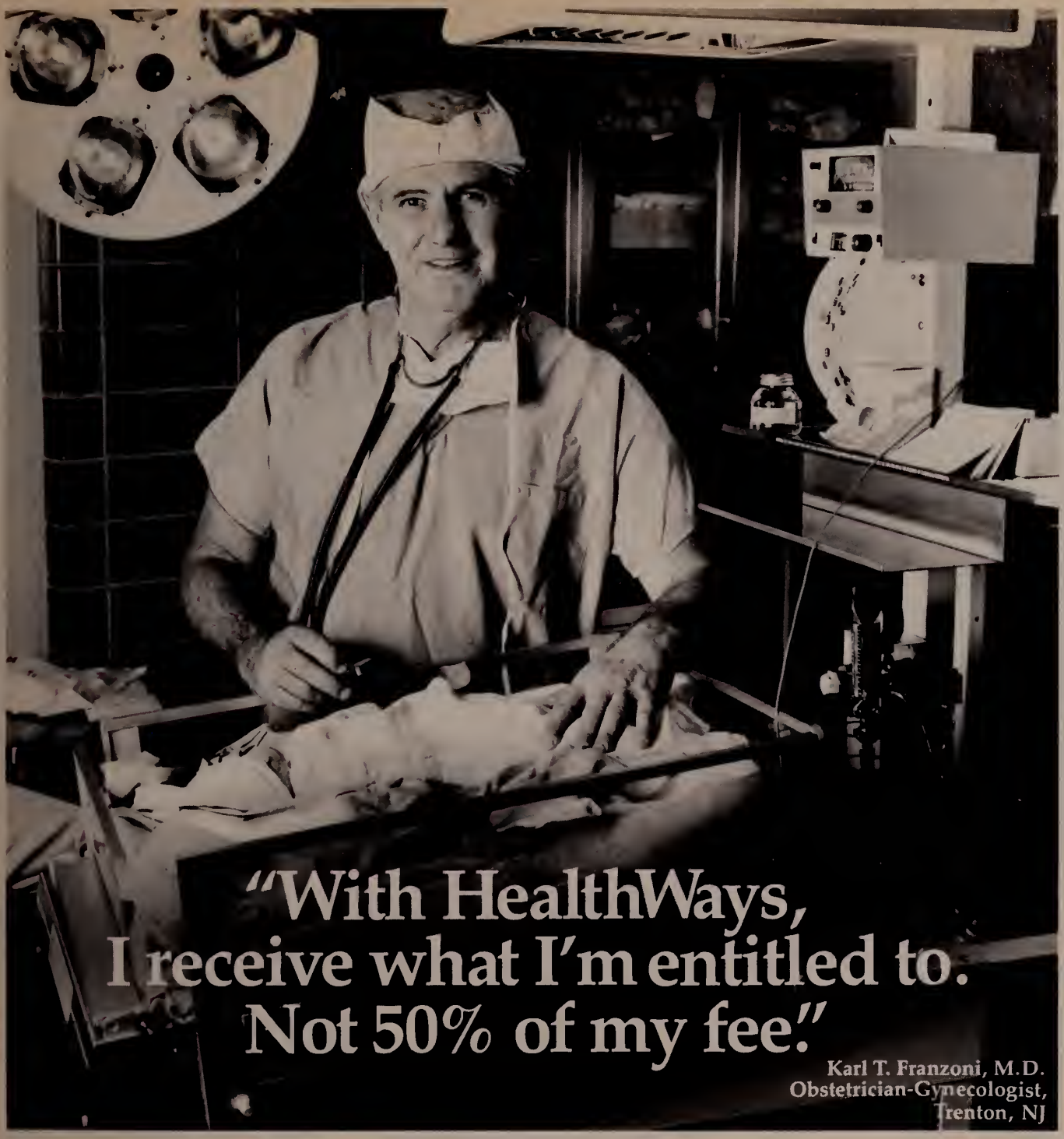
WESTCHESTER

June 12. **Update on Malignant Hypertension.** 1 Cat 1 Credit. Info: Jodi Horton, Director, Public Relations and Development, St Joseph's Medical Center, 127 South Broadway, Yonkers, NY 10701. Tel: (914) 965-6700, ext. 535.

MONROE

June 5–6. **Fourth Annual Update in Critical Care.** Info: University of Rochester Medical Center, Office of Continuing Professional Education, 601 Elmwood Ave, Box 677, Rochester,

(*Continued on p 13A*)



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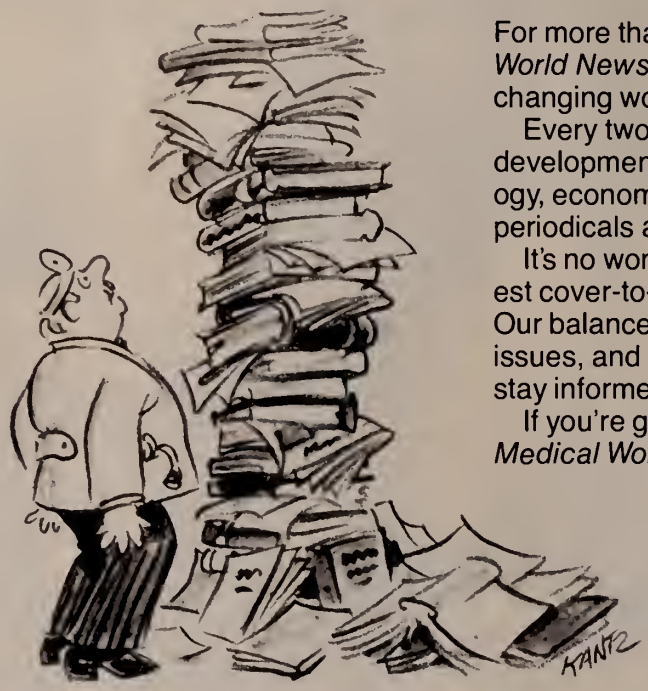

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BIOTECHNOLOGY LAW: Irwin Birnbaum and Paul J. Giancola, Lawyers, Mony Tower II, Syracuse, New York 13202, 315/422-0246 (In New York, 800/358-8568), biotechnology and scientific litigation. Regulatory affairs; negotiation of patent rights with major corporations and investors. Experienced in negotiations involving chemonucleolysis bone growth stimulation, and other modalities. Irwin Birnbaum and Paul J. Giancola, Mony Tower II, Syracuse, New York 13202, 315/422-0246 (In New York, 800/358-8568).

Give your angina patient added protection...

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- ***Proven efficacy when used alone in angina[1, 4-6]***
- ***Compatible with both beta-blockers and nitrates[7]***

Please see brief summary of prescribing information on the next page.

CARDIZEM® 60 mg tid or qid

diltiazem HCl/Marion

FEWER SIDE EFFECTS IN ANTIANGINAL THERAPY

BRIEF SUMMARY

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist).

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM (diltiazem hydrochloride) in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** — CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

CARDIZEM 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other. Issued 4/1/84

See complete Professional Use Information before prescribing.

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COMMENTARIES

Descriptive epidemiology and cancer control

The National Cancer Institute (NCI) has recently proposed a goal of reducing cancer mortality in the United States 25 to 50% by the year 2000.[1] These reductions are to be achieved through effective and more extensive application of existing and emerging primary, secondary, and tertiary prevention strategies. Primary prevention objectives emphasize the need to further reduce the proportion of the population using tobacco products. The year 2000 objective is to reduce the percentage of adults who smoke from 34% to 15% or less, and to reduce teenage smoking from 36% to 15% or less. Reducing the amount of fat in the diet from 40 to 25% or less of the total daily caloric intake and increasing fiber intake are also important primary prevention objectives. Secondary prevention objectives focus on increasing the proportion of women who receive periodic screening for cancers of the breast (mammography and clinical examination) and cancers of the uterine cervix (pelvic examination and cytology). Extension of state of the art therapy to all segments of the population is the key tertiary prevention objective.

The identification of specific, quantifiable end points provides a useful framework for developing new and potentially more effective cancer control programs. Achievement of the NCI goals and objectives will depend on a number of factors including the ability to identify high risk segments of the population that may benefit from targeted cancer control interventions. High risk populations also provide a focus for future cancer control research.

The use of descriptive epidemiology to develop site-specific cancer risk profiles is well illustrated in the article by Brandys and associates[2] that appears in this issue of the *Journal*. The authors examined cancer mortality rates in ten health districts of Kings County (Brooklyn), New York for the years 1980 through 1983.

Overall, cancer mortality was shown to be significantly lower in three health districts and above average in one district when compared to data from the National Cancer Institute's Surveillance, Epidemiology, and End-Results Programs (SEER).[3] More importantly, a number of intriguing site-specific excesses were observed for residents of Kings County. Deaths from cancers of the hepatobiliary system, stomach, breast, and non-Hodgkin's lymphomas and malignant melanomas were observed to be significantly elevated in this population.

The authors suggest that excess mortality for cancers of the liver and stomach and non-Hodgkin's lymphomas may be concentrated in the large and ethnically diverse migrant population living in Kings County. Migrant populations often maintain the cancer risk patterns characteristic of their place of origin. This tendency for some migrant groups to maintain either high or low cancer risk profiles may indicate a genetic influence or an important role for environmental factors, which exert their influence early in life. The tendency for many migrant groups to maintain certain cultural and lifestyle practices such as diet also needs to be considered. Information concerning age at migration may aid in determining the validity of these interpretations.[4] This latter interpretation suggests that opportunities for active intervention may still be possible in populations with a clearly identified risk of developing specific cancers.

Factors that may play an important etiologic role in these excesses are also discussed. The authors suggest that the high hepatocellular cancer mortality rates observed in Kings County may be associated with groups of persons who migrate from areas of the world where a large percentage of the population are carriers of hepatitis B virus. The potential etiologic importance of widespread intravenous drug use in urban areas like Kings County is also discussed.

Previous research[5] has also shown elevated stomach cancer risks in several of the migrant groups represented in the Kings County population. This disease has also been linked to low socioeconomic status,[6] and life-long dietary patterns have been investigated as possible causes of this form of cancer.[7]

Haenszel[8] has also shown that non-Hodgkin's lympho-

mas occur more frequently than expected in migrants from eastern Europe. The authors suggest that Jewish migrants from the Soviet Union may contribute significantly to the high number of non-Hodgkin's lymphoma deaths observed in Kings County.

Breast cancer mortality was also observed to be significantly above average in Kings County. Data from various sources have shown high breast cancer mortality rates and poor survival to be associated with race[9,10] and socioeconomic status.[11] Breast cancer survival rates are lower in blacks and lower socioeconomic groups when compared to whites and more affluent women. One recent study[12] suggests that socioeconomic status may be a more important determinant of breast cancer survival and mortality patterns than race or ethnicity. The link between sociocultural factors and breast cancer mortality in Kings County is suggested by the area's low level of affluence relative to the other boroughs of New York City. The NCI is currently sponsoring a number of analytic studies that may help to determine the relative contribution of biologic, cultural, and medical care factors to these mortality patterns.

As epidemiologic methods have become more mathematically sophisticated, there has been a tendency to forget the basic roots of the epidemiologic approach. Basic descriptions of the relationships between disease occurrence and the characteristics of person, place, and time remain the fundamental building blocks of epidemiology. Descriptive analysis is an essential tool in hypothesis development that guides analytic studies. The ultimate goal of primary prevention is dependent on the effective interface of descriptive and analytic epidemiology. The paper by Brandys and colleagues[2] is an excellent example of the role of descriptive epidemiology as a first step in the formation of cancer control strategies.

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Pleomorphic adenomas of the breast

Mixed tumors, as a class, pose interesting questions in both definition and understanding. Some tumors are simultaneous proliferations of more than one element of a tissue, as in the mammary fibroadenoma with its epithelial and stromal elements; others represent metaplastic change in one or more of the proliferating cell types. On occasion, metaplasia or redifferentiation occurs within the accepted potentials of the particular germ cell family represented (as in osseous or cartilagenous metaplasia in the stroma of cystosarcomas of the breast). It is more difficult to understand those examples in which metaplasia transgresses orthodox pathways of differentiation, such as when epithelial cells develop mesodermal properties as in mixed tumors of the breast. Indeed, sharp separations between cell types become more and more difficult as it is realized that all cells share the same 46 chromosomes, that very few cells have qualitatively distinctive organelles by electron microscopy, and that functional properties, as illustrated by ectopic hormone production, may equally deviate from what would be expected.[1] Some normal cells, such as myothelium, share epithelial and connective tissue qualities, as reviewed by Dardick and associates.[2]

The article by Segen and colleagues[3] in this issue of the *Journal* deals directly with these problems in reporting a case of pleomorphic adenoma of the breast with positive estrogen receptors and positive S-100 immunohistochemi-

cal staining. Neither of these studies has been previously performed on such tumors.

Pleomorphic adenomas (mixed tumors) of the human breast with an identical histologic pattern to that of salivary glands are rare. They are benign tumors, first recognized and described in the French literature by Lecène in 1906[4] and later by Nabert and co-workers in 1968.[5]

In our report of a case and a review of the literature in 1975,[6] we believed that histologically similar tumors were assumed to have been first reported in the English literature by Smith and Taylor in 1969.[7] However, these authors considered the tumors to represent intraductal papillomas with stromal metaplasia. This view has subsequently been shared by other authors including McClure and Smith,[8] who did not identify these tumors as pleomorphic adenomas in their review of the literature, and concluded that by 1982 only six undisputed cases of pleomorphic adenomas of the breast had been reported in the literature.

At the time of our report,[6] the predominant benign nature and biologic behavior of these tumors was not recognized and appreciated, and a number of patients underwent unwarranted extensive surgery. Recurrences of rare malignant mixed tumors have been reported.[6,8] A multicentric origin of the tumor, although rare, or incomplete removal of the tumor, especially if satellite lesions are present, might provide a ready explanation for the recurrences. This is not an unusual occurrence in pleomorphic adenomas of salivary glands, particularly of the parotid.

Segen and associates[3] and others favor a major role of the myoepithelial cell in the morphologic characteristics and directional differentiation in these tumors. The biphasic myoepithelial differentiation in pleomorphic adenomas has been demonstrated by ultrastructural studies.[8,9] The positive immunohistochemical staining for S-100 demonstrated in normal breast myoepithelial and epithelial cells and in this tumor confirms the myoepithelial component in pleomorphic adenomas and supports the epithelial derivation of such cells.

The significant contribution of the present case report[3] is the positivity of this tumor for estrogen receptors. Estrogen receptors are present in normal, hyperplastic, and malignant breast epithelial cells. It has been shown that in benign breast lesions (eg, fibroadenoma), high estrogen levels reflect increased cellularity of the lesion and the patient's age (ie, young individuals).[3] The high level of estrogen receptors in the present case is unusual in view of the patient's age and the relative paucity of the epithelial component, since the proportion of stromal component appears to influence the amount of extracted estrogen.[10] In his cytochemical study of estrogen receptors in human mammary cancer, Lee[10] also emphasized that the amount of estrogen receptors in cytosol protein of tumor tissue homogenate was influenced in part by the size of the epithelial component. In addition, in this study frozen sections from both fibroadenoma and gynecomastia of the breast, stained for estrogen receptors, showed moderately increased estrogen binding not only in the epithelial cells but also in the stromal cells.

How may the presence of abundant stroma and myoepithelial component in pleomorphic adenomas be reconciled with the high estrogen binding in the tumor reported by Segen and colleagues[3]? A plausible explanation may be that the myoepithelial and stromal cells contribute to the positive estrogen receptor content. This is supported by the extensive study and review by Dardick and coworkers[2] in which they concluded that the myoepithelial cell in the salivary gland is of ectodermal origin; an epithelial-derived cell with the potential for multidirectional differentiation. Ultrastructurally, in pleomorphic adenomas of the salivary glands, the stromal cells show epithelial cell features. Similarly, ultrastructural studies of infiltrating ductal carcinomas of the breast, as quoted by these authors, have identified cells with both secretory and myoepithelial features. It is therefore highly likely that the myoepithelial and stromal cells in pleomorphic adenoma of the breast express the ability of estrogen binding by gene derepression during neoplastic cell proliferation.

Estrogen receptor assays on cytosol preclude morphologic identification of the positive specific cells. However, an immunoperoxidase method for estrogen receptor staining on frozen sections has recently become available. A study by King and associates[11] on the comparison of immunocytochemical and steroid-binding assays for estrogen receptors in human breast tumors showed a good association between the nuclear immunostaining of breast tumors with monoclonal antibodies to the estrogen receptor protein and the concentration of cytosolic estrogen receptor. In this study, as in that by Lee,[10] epithelial cellularity showed the highest degree of correlation with the results of the steroid-binding protein.

The availability of these monoclonal antibodies and the application of immunocytochemical techniques in the study of pleomorphic adenomas will allow for the identification of cells with localization of the receptor nuclear content. Possible future studies on pleomorphic adenomas may aid in defining the role of the myoepithelial and stromal cells, if any, in the positive estrogen binding in these tumors.

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Primary carcinoma of the urethra in men

Primary carcinoma of the male urethra is a rare disease. Only a few hundred cases have been reported in the world literature. The cause of the disease is unknown, and no institution has had enough experience with the disease to formulate the best therapeutic modalities. Nearly 80% of carcinomas of the male urethra are squamous cell tumors. Transitional cell carcinomas, which are usually located in the prostatic urethra, represent 15%; 5% belong to the adenocarcinoma group.[1]

Although the cause of the disease is unknown, most patients with urethral carcinoma have a history of prior urethral stricture, multiple transurethral procedures, or other endoscopic manipulations. The majority of patients are diagnosed only after significant delay.

The current staging system for carcinoma of the urethra combines clinical and pathologic features: 0, carcinoma in situ; A, into but not beyond the lamina propria (submucosa); B, into but not beyond the substance of the corpus spongiosum or into but not beyond the prostate; C, direct extension beyond the corpus spongiosum (corpora cavernosum, muscle, fat, skin, bone, and fascia) or beyond the prostatic capsule; D1, regional metastases, including inguinal and pelvic lymph nodes; and D2, distant metastases. The prognosis is closely related to the stage of the disease. In general, the prognosis for carcinoma of the urethra is poor because nearly 70% of patients are initially seen in the advanced stage, usually stage C.[1]

In this issue of the *Journal*, Sawczuk and associates describe what appears to be a stage C tumor.[2] Surgical therapy in this particular patient will not likely improve length of survival, but it will improve quality of life. Some recent reports indicate that radiotherapy alone may be curative or may essentially improve the prognosis in patients with early or moderately advanced disease. For more advanced stages, a combination of preoperative radiation followed by radical surgery (usually requiring an en bloc removal of the urethra, urogenital diaphragm, prostate, seminal vesicles, and bladder) is recommended.[3-5] For a clean surgical margin, resection of the inferior rim of the pubis must be performed as well.

The best approach to the therapeutic dilemma for patients with urethral carcinoma is early detection. Therefore, all patients with a history of urethral stricture or frequent intraurethral manipulation should be routinely evaluated with cytology, urethroscopy, and biopsy if a suspicious lesion is found.

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The geographic distribution of cancer mortality in Kings County, New York 1980–1983

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ABSTRACT. Cancer mortality in Kings County (Brooklyn) was studied for the years 1980 to 1983. Standardized mortality ratios adjusted for age, sex, and race were computed for the 16 most common sites in each of the ten health districts. Total cancer mortality was significantly lower in three health districts and higher in one when compared to a large national series (SEER). Differences in the remaining districts were inconclusive. While overall risk of death was similar in both the national and the Kings County series, risk varied by site of disease. Mortality from cancers of the hepato-biliary system and stomach were much higher in Kings County residents than nationally. Mortality was also significantly higher for breast cancer, non-Hodgkin's lymphomas, malignant melanoma, and other forms of skin cancer. Possible reasons for these findings are discussed.

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It has been demonstrated that significant differences in cancer mortality patterns exist among geographic regions.[1–5] This variation has been useful for identifying risk factors and specific population groups for further epidemiologic evaluation.

In the United States, cancer mortality has been mapped at both state and county levels. The heterogeneity of populations in many states limits the value of statewide data. Hoover and associates[6] suggest that the county is well suited as a basic geographic unit for epidemiologic investigation, since it represents an area small enough to be homogeneous for demographic and environmental characteristics that might influence cancer risk, and yet large enough to provide stable estimates of site-specific cancer mortality. However, this is not true of the counties in New York City.

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Kings County (Brooklyn), one of the five counties of the City of New York, with a population of 2.2 million, is larger than 16 states and equal in size to six other states. The county's population is a mosaic of racial, ethnic, and socioeconomic groups. Moreover, the county contains both industrial and residential areas.

Consequently, the first step in evaluating the cancer mortality pattern of Kings County was to divide the county into small geographic areas. In this way it was possible to identify more homogeneous areas that may significantly contribute to the overall mortality of the county.

Mortality patterns provide clues for the etiologic determinants of cancer and therefore for cancer prevention.[7,8] A systematic approach to the analysis of cancer mortality patterns utilizing the principals of epidemiology is important for effective cancer control at the local level. The data available for exploring cancer mortality in densely populated, small geographic areas represent an unexploited resource for epidemiologic investigations. While this study is exploratory in nature, specific etiologic hypotheses are suggested by the results.

This report describes the pattern of cancer mortality during the period of 1980 to 1983 in the ten health districts that comprise Kings County. In New York City, health districts are the administrative areas for which standard vital statistics, including births and deaths, are reported.

PATIENTS AND METHODS

The population data for health districts used in this study were derived from the New York City Department of Health's Office of Epidemiologic Surveillance and statistics from the 1980 census. Data for site-specific primary cancer deaths were provided by the Bureau of Statistics and Analysis of the New York City Department of Health. For the purposes of this study, 16 of the most common sites were chosen for evaluation.

Since mortality varies with age, sex, and race, rates were adjusted by these factors and standardized mortality ratios (SMRs) were computed. An indirect standardization was used to calculate the SMRs.[9] In this approach age, sex, and race specific rates for a national series of data reported by the Surveillance,

Epidemiology, and End Results (SEER) program were used as the standard.[10] The SEER program is composed of several population-based tumor registries that encompass some 25 million people or approximately 10% of the US population. Although this is a substantial sample, it is not necessarily representative of the national population. Nonetheless, it includes several states and large cities and offers a fairly broad cross-section for comparison of both cancer mortality and morbidity.

The number of expected deaths from cancer was calculated for age, sex, and race specific subgroups in each of the ten Kings County health districts by applying the SEER rates to the district's population. The expected number of deaths in each population subgroup were summed to get the total number of expected deaths in a district. Expected deaths in the county were obtained by summing the results across the ten health districts. The expected deaths were then compared to the observed deaths by forming a mortality ratio. This procedure was repeated for each site.

If no difference existed in cancer mortality in Kings County as compared to the national population, then the SMR was unity. Variation from unity measures the extent to which cancer mortality is either higher or lower in residents of Kings County. Random fluctuation in the number of observed deaths was minimized by using data that covered a four-year period. The Poisson test was used to calculate 95% confidence intervals for the SMRs.[11] The confidence intervals represent limits that would encompass random or chance fluctuation in the SMRs. If the confidence interval includes one, then chance cannot be ruled out as being responsible for the observed difference in the SMR. However, if the confidence interval for a SMR does not include one, then it is reasonably certain that the occurrence of that cancer in residents of Kings County differs significantly from the national experience.

Summary-adjusted SMRs were used to increase the reliability of the estimated ratios and to reduce multiple comparison bias. Examination of specific sites among the health districts was limited to four sites that differed for the county as a whole. Improved reliability is one of the major advantages of using indirect rather than direct standardization; that is, the use of more reliable specific rates that are based on a standard population that is greater than ten times the population of Kings County.[12] Additionally, the indirect approach may be applied without age, sex, race, and site specific death rates for each health district in the county. The failure to detect differences that may exist among the strata being adjusted and incomplete adjustment for differences in population composition are two disadvantages of utilizing the indirect approach. However, in the present study, the significant differences in specific cancer (except melanoma) mortality found for all Kings County residents are consistent with an earlier report using the direct method of standardization.[13]

The possibility exists of multiple comparison bias in exploratory analyses of the present type. This bias occurs when many hypotheses are tested and some differences occur due to chance alone. In the present study, 56 SMRs were examined for statistical significance, including mortality for four sites for the ten health districts plus mortality for 16 sites for Kings County as a whole. If 5% were significant due to chance, then three of our significant results would be incorrect.

TABLE I. Kings County Population by Sex, Race, and Health District—1980 (%)

Health district	Sex		Race		
	Male	Female	White*	Black	Other
Bay Ridge	46.0	54.0	96.4	0.4	3.2
Bedford	44.7	55.3	10.2	88.2	1.6
Brownsville	45.3	54.7	46.1	51.6	2.3
Bushwick	45.4	54.6	65.6	32.1	2.3
Flatbush	45.8	54.2	62.4	33.8	3.8
Fort Greene	45.8	54.2	34.5	63.2	2.3
Gravesend	46.2	53.8	90.9	6.7	2.4
Red Hook-Gowanus	48.8	51.2	77.8	19.1	3.1
Sunset Park	47.2	52.8	92.6	2.4	5.0
Williamsburg-Greenpoint	47.6	53.9	90.2	7.3	2.5

* Includes the Hispanic population.

Table II. Kings County Population by Health Districts and Age Groups—1980 (%)

Health district	Age group*					
	0–14	15–34	35–54	55–64	65+	Total
Bay Ridge	16.8	30.2	21.0	13.0	19.0	249,112
Bedford	26.2	34.1	23.3	8.6	7.9	208,653
Brownsville	27.5	34.5	21.6	8.5	7.9	271,206
Bushwick	31.3	34.6	19.7	6.9	7.5	166,602
Flatbush	21.5	33.7	21.6	10.0	13.0	479,523
Fort Greene	25.5	37.4	21.7	7.4	8.0	146,739
Gravesend	16.7	28.9	20.2	13.9	20.3	287,940
Red Hook-Gowanus	20.0	38.1	22.6	8.9	10.5	114,345
Sunset Park	24.8	32.8	18.8	10.0	13.6	164,477
Williamsburg-Greenpoint	27.1	32.6	19.8	10.2	10.3	142,403

* In the standardization, five-year age intervals were used.
Source: 1980 US census.

RESULTS

Demographics. The ten health districts in Kings County are shown in the Figure and the sex and race distribution for each health district is shown in Table I. All ten districts display a female predominance. The county's white population is concentrated in the southern tier, while the black population is largely concentrated in the central and eastern portion of the county. The Hispanic population, which is widely dispersed throughout the county, is counted as part of the white population in this study.

Table II shows the age distribution for each health district. A clear geographic pattern exists with respect to the age distribution of

FIGURE. Depiction of the ten health districts in Kings County (Brooklyn) of New York City.

Table III. Mean Yearly Cancer Deaths and Cancer Mortality Rates in Kings County by Health Districts, 1980 to 1983

Health district	Population	Observed deaths	Rate/100,000	Expected deaths	Standardized* mortality ratio
Bay Ridge	249,112	628	252.1	675	0.93
Bedford	208,563	384	184.0	365	1.05
Brownsville	271,217	421	155.2	416	1.01
Bushwick	166,609	243	145.9	226	1.08
Flatbush	479,533	922	192.3	988	0.93†
Fort Greene	146,739	259	176.5	230	1.13†
Gravesend	287,940	768	266.7	841	0.91†
Red Hook-Gowanus	114,345	194	169.7	197	0.99
Sunset Park	164,477	290	176.3	333	0.87†
Williamsburg-Greenpoint	142,403	239	167.8	240	1.00
Kings County	2,231,028	4,348	194.9	4,511	0.97

* Standardized for age, race, and sex using (SEER) results (1973–1977).
† $P < 0.05$.
Source: 1980 US census and the New York City Department of Health, Bureau of Statistics and Analysis.

the county. Approximately one third of the population under 18 years of age is concentrated in the central and eastern portion of Kings County, while the county's elderly population is concentrated in the southern tier.[14] There is a close correlation between age and race. The vast majority of the county's senior citizens are white, while the population under 18 years of age is mainly comprised of blacks and Hispanics.

Mortality. During the four-year period under investigation there was a total of 17,392 cancer deaths; an average of 4,348 deaths per year. Table III shows the mean annual number and expected cancer deaths for each of the ten health districts in Kings County. The average annual death rate for residents of the county was 20% higher than the rate for the SEER population—194.9 per 100,000 as compared to 165.1 per 100,000. When the rate was adjusted for age, race and sex, overall cancer mortality in Kings County was almost identical to the national figure. Despite this similarity, there was substantial variation by site and health district.

An excess in cancer mortality for all sites was found in three contiguous health districts—Fort Greene, Bedford, and Bushwick—but was statistically significant only in Fort Greene ($P < 0.05$). For three health districts—Flatbush, Gravesend, and Sunset Park—cancer mortality for all sites was significantly less than the national series ($P < 0.05$). Differences in the remaining districts were inconclusive. While overall risk of death was similar in both the national and the Kings County series, risk varied by site of disease. Table IV shows that the SMRs were significantly elevated for cancer of the hepatobiliary system, stomach, breast, lymphoma, melanoma, and other skin cancer and significantly reduced for cancer of the prostate ($P < 0.05$).

The most striking excess occurred for cancers of the hepato-biliary system, a rare disease in the United States. Residents of the county had a 70% excess of mortality from hepato-biliary malignancies. The excess was significantly elevated for every health district but Sunset Park, and was most pronounced in Bushwick and Fort Greene (Table V).

Overall there was a 26% excess in mortality due to stomach cancer. Mortality was above the expected levels in nine of the ten health districts with the excess statistically significant for Bedford, Brownsville, Fort Greene, Gravesend, Sunset Park, and Williamsburg-Greenpoint ($P < 0.05$).

Mortality due to breast cancer was 7% higher in women in Kings County than in women of comparable age and race in the national

Table IV. Standardized Cancer Mortality Ratios for Kings County Residents, 1980 to 1983

ICD		Deaths Observed	Deaths Expected	Standardized* mortality ratio	95% Confidence interval
162	Trachea, bronchus, and lung	3,691	3,804	0.97	0.94–1.01
153–154	Colon-rectum	2,419	2,512	0.96	0.92–1.01
174	Breast	1,730	1,616	1.07†	1.01–1.13
157	Pancreas	963	940	1.02	0.95–1.10
185	Prostate	856	984	0.87†	0.81–0.94
151	Stomach	864	684	1.26†	1.17–1.37
188–189	Bladder and others	711	748	0.96	0.88–1.05
155–156	Liver and others	645	380	1.70†	1.55–1.86
204–208	Leukemia	634	600	1.06	0.97–1.16
200–202	Lymphoma	590	520	1.13†	1.03–1.25
203	Multiple myeloma	268	236	1.13	0.99–1.26
183	Ovary and other uterine adnexa	454	456	1.00	0.89–1.11
180	Cervix uteri	215	248	0.87	0.74–1.02
182	Corpus uteri	109	100	1.09	0.87–1.36
140–149	Lip, oral cavity, and pharynx	358	320	1.12	0.99–1.26
172–173	Melanoma and skin	207	148	1.40†	1.19–1.64
	All sites	17,392	18,044	0.97	0.94–1.00

* Standardized for age, race, and sex using SEER results (1973–1977).
† $P < 0.05$.

Table V. Observed, Expected, and Standardized Mortality Ratios* For Selected Cancer Sites by Health Districts, 1980 to 1983

Health district	Liver/Gallbladder Observed/Expected	SMR	Stomach Observed/Expected	SMR	Breast Observed/Expected	SMR	Prostate Observed/Expected	SMR
Bay Ridge	99/64	1.55†	118/108	1.13	259/248	1.05	116/152	0.76†
Bedford	46/24	1.92†	81/60	1.35†	142/120	1.18	126/88	1.43†
Brownsville	55/32	1.73†	92/60	1.53†	162/156	1.04	72/84	0.86
Bushwick	36/12	3.00†	43/32	1.35	96/84	1.14	53/40	1.33
Flatbush	153/92	1.67†	160/160	1.00	414/364	1.14†	178/212	0.84†
Fort Greene	42/12	3.50†	56/36	1.56†	103/80	1.27†	59/48	1.23
Gravesend	106/84	1.26†	159/132	1.21†	313/296	1.06	133/200	0.66†
Red Hook-Gowanus	29/12	2.43†	26/20	1.30	73/68	1.08	44/36	1.22
Sunset Park	37/24	1.16	70/48	1.46†	101/116	0.87	47/76	0.62†
Williamsburg-Greenpoint	43/16	2.70†	59/32	1.85†	80/84	0.95	28/48	0.58†

* Standardized for age, race, and sex using SEER results (1973–1977).
† $P < 0.05$.

series ($P < 0.05$). While eight health districts displayed an excess mortality, the excess was significant only in Flatbush and Fort Greene.

In Kings County, a 40% excess in mortality from malignant melanoma and other forms of skin cancer and a 13% excess in mortality from lymphoma were also significantly higher than in the national series. However, the number of cases for these two malignancies was too small to examine the variation among the ten health districts.

For prostatic cancer, mortality was 13% lower than the national level ($P < 0.05$). However, this mortality ratio was a combination of an excess mortality in four of the ten health districts with large black populations and a deficit in the others. In Bedford, the excess was statistically significant, whereas in Bay Ridge, Flatbush, Gravesend, Sunset Park, and Williamsburg-Greenpoint, the deficit was significant ($P < 0.05$).

Excess mortality from multiple myeloma and cancer of the oral cavity, and a deficit in mortality from cervical cancer were also evident among residents of Kings County. However, these differences from the national population were not statistically significant.

Discussion

While overall cancer mortality for residents of Kings County displayed little difference from the SEER population, great variation existed between the two populations in mortality from specific anatomical sites. In 1980, it was estimated that 23.8% of the county's residents were foreign born, an increase of one third over the previous decade.[14] The single largest group to migrate to Kings County was from the Caribbean basin. There was also significant immigration from Latin America, Italy, Poland, and the Soviet Union. It is highly likely that this figure underestimates the foreign-born population since the impact of undocumented immigration is impossible to gauge. The observed differences in cancer mortality patterns between the residents of Kings County and the SEER population, in at least three cancer sites, may be due to cancer risks of migrant populations. The most striking difference between the two populations is the excess mortality from cancers of the hepato-biliary tract observed in residents of Kings County. While primary liver cancer is a leading cause of death in parts of Asia and Africa, it is relatively uncommon in the United States. Cancers of the biliary tract are common in central and eastern Europe and Latin America whereas in the United States these sites account for only 1% of all cases.[15]

In the years between 1960 and 1979, Kings County experienced a substantial rise in deaths from cancers of the hepato-biliary tract among all race and sex groups, but the increase was most pronounced in the nonwhite population. Riggan and colleagues[13] reported a 95% increase in mortality from cancers of the liver and gallbladder among nonwhite men in Kings County. For nonwhite women there was a 48% increase. Among white residents, there was a 61% increase among men and a 12% increase among women.

In the 1950s, Newill[16] observed an excess of mortality from liver cancer among the foreign-born white populations of New York City in contrast to an earlier report by MacMahon[17] who found an increase in this site in the city's native white population.

The areas of the world with a high prevalence of hepatitis B virus carriers are those with the highest incidence of primary hepatocellular carcinoma. The excess risk of developing this cancer among carriers of the virus has been found to be more than 200 times greater than expected in a prospective study in Taiwan.[18] Prince and Alcabes[19] found a ten-fold increased risk of the neoplasm among carriers of the hepatitis B virus in New York State. This suggests that the excess mortality from cancer of the hepato-biliary tract is due to migration from high risk areas to Kings County. The widespread drug abuse characteristic of many of our major cities may also be a contributing factor.

The excess in mortality from stomach cancer may also be explained by immigration. Both MacMahon[17] and Newill[16] found that mortality from gastric cancer was higher in the foreign-born white population than in the native white population of New York City during the 1950s. Although Terris and Hall[20] reported a decline in stomach cancer mortality in New York City between 1949 to 1951 and 1959 to 1961, they found that the decreased mortality could not be attributed to a decline in the foreign-born population. The decline was greatest in those groups with the lowest initial rates. These studies suggest that the risks of stomach cancer are either encountered early in life, or that factors influencing risks for stomach cancer persist and carry over unchanged in the migrants' adopted country. The persistence of dietary patterns is one possibility.

Epidemiologic studies have demonstrated a clear relationship between stomach cancer and low socioeconomic status.[21] In Kings County, white, black, and Hispanic

families all earned less than the citywide median income for their respective racial and ethnic groups.[14] Immigration, socioeconomic status, and dietary habits are all highly correlated and may account for the excess mortality in stomach cancer either separately or in combination.

Non-Hodgkin's lymphoma is the third type of cancer for which migration from high risk areas provides an explanation for the excess mortality observed in residents of Kings County. In a study of cancer mortality among the foreign-born white population of the United States in 1950, Haenszel[22] noted above average lymphoma risks for both sexes among migrants from the Soviet Union, Poland, and Austria. MacMahon[17] found an excess risk in all lymphoma categories among Jews in New York City during the 1950s. Since a substantial proportion of Jews migrated from Russia, a classification by religion or country of birth would be related for that group, so that the finding of excess lymphoma mortality for Jews would be consistent with the high risk evident in the national data for migrants from Russia.

Cantor and Fraumeni[23] found that mortality rates for non-Hodgkin's lymphoma in counties of the contiguous United States from 1950 to 1975 were consistently elevated for men in counties with high percentages of residents of Russian or Greek descent. This suggests that the increased mortality from non-Hodgkin's lymphoma in Kings County reflects the increased migration of Jews from the Soviet Union during the past decade.

Survival rates have been consistently better for white patients with cancer than for black patients for most major anatomical sites.[10] Berg and coworkers[25] suggest that differences in socioeconomic status explain the poor survival rates among black patients with cancer. Patients from low income groups generally fare worse than their more affluent counterparts. Since blacks tend to be concentrated more in the low income strata of the population, their survival will be poorer. Among patients with breast cancer, the survival advantage for white women is maintained within categories of stage at diagnosis, indicating that more advanced disease at time of diagnosis cannot entirely account for the survival differential between the races.

Dayal and associates[26] found in a study of breast cancer survival in Richmond, VA, that racial differences are insignificant when adjustment is made for socioeconomic status. The difference in survival among different socioeconomic groups persists even after adjustment is made for stage at diagnosis. One would expect that if blacks and whites had similar incomes, survival differences would diminish. Because the population of Kings County is less affluent than the rest of New York City, the excess breast cancer mortality may be due to the higher case fatality rate observed in low income groups.

There is no apparent explanation for the excess mortality due to malignant melanoma and other forms of skin cancer. The dominant risk factor, exposure to ultraviolet radiation from the sun, occurs less frequently in Kings County than in many other parts of the country.

Very often statistical averaging masks significant variation. This appears to have happened with prostatic cancer. While there was a significant deficit in mortality from prostate cancer for the county as a whole, the deficits are primarily found in those health districts with a substantial white population. Differences existed among health districts in Kings County despite the fact that the SMRs were standardized for race. This is consistent with a report by Blair and Fraumeni[27] that found that mortality for prostatic cancer was about 50% higher in all parts of the United States where blacks comprise most of the nonwhite population. They also found that mortality rates for nonwhites rose sharply with increasing population density. However, in a study of population density and cancer incidence in upstate New York, Nasca and colleagues[28] found no association for cancer of the prostate.

The excess mortality found in health districts with substantial black populations is most likely to be due to blacks presenting with more advanced disease at diagnosis and higher case fatality rates.[29] MacMahon[17] and Newill[16] found Jews in New York City to have the lowest death rate from prostatic cancer among the three major religious groups. The deficits in cancer of the prostate may be attributable to the large concentrations of Jewish residents in the southern part of the county, as well as in the Williamsburg-Greenpoint health district, which is home to a substantial Hassidic population.

It should be emphasized that the results obtained from this research might differ if cancer occurrence were substituted for mortality. A higher case fatality could produce excessive mortality, even in the absence of excessive occurrence. However, for cancer of the hepato-biliary tract and cancer of the stomach, case fatality is very high and so incidence and death rates will be similar. The reliability and accuracy of death certificate diagnosis varies, and some of the deaths attributed to primary liver cancer may have resulted from metastases from other primary sites. This would erroneously produce an excess mortality for liver cancer. However, there is no reason to believe that death certification in New York City is less accurate than for the SEER program.

Mortality data are not always precise measures; however, they are very useful in suggesting etiologic clues to be investigated by subsequent studies with more powerful research designs. Before such studies may be undertaken there is considerable need to examine cancer mortality patterns in small geographic units and subpopulations in large cities such as New York. Such studies can provide community profiles that will enhance local cancer control initiatives.

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See also pp 231–232.

THE FIORELLO H. LAGUARDIA ARCHIVES

The Fiorello H. LaGuardia Archives of LaGuardia Community College of the City University of New York is producing a series of eight public radio programs on the LaGuardia years (1934 to 1945) in New York City. One of the programs will focus on the expansion of public health services in the city during this period. For the program, the Archives would like to interview physicians, administrators, or other health care professionals who were associated with the New York City Department of Health district health centers from 1934 through 1945. Please contact Richard Barr, LaGuardia Archives, LaGuardia Community College, 31-10 Thomson Ave, Long Island City, NY 11101. Tel: (718) 626-5078.

Fine needle biopsy of thyroid nodules: Avoiding the pitfalls

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This review presupposes rejection of both the obsolete philosophy that all thyroid nodules must be excised to prevent the morbidity and mortality of thyroid cancer; and the recently published[1] nihilistic notion that it makes no difference whether thyroid nodules are treated surgically, with thyroxine, or studied by needle biopsy. Fine needle biopsy (FNB) makes sense only for physicians who believe that limiting surgery to the minority of patients with higher risk nodules, and observing the rest, will minimize the morbidity and mortality of thyroid cancer, and the risks and costs of surgery. Thyroidologists,[2-5] pathologists,[6-8] and even many surgeons[9-11] agree that any combination of other methods of thyroid nodule evaluation—including history, physical examination, thyroid function tests, antithyroid antibody determinations, trial of treatment with thyroxine, thyroid imaging, and echography—is substantially less accurate than FNB, and leads to too much unnecessary surgery.

The unreliability of clinical evaluation, including suppression with thyroxine, provided the impetus for nuclear imaging. Nodules with increased function may be safely considered benign.[12] However, most nodules are hypofunctional (cold). Although most malignancies present as cold nodules, more than 90% of cold nodules are benign. Hence operation for all cold nodules is a prescription for nearly as much unnecessary surgery as would result from operation for all nodules. Thus thyroid imaging eliminates concern for a small proportion of thyroid nodules, but cannot establish a diagnosis of malignancy for any. Some physicians think it is cost-effective to use FNB as the initial diagnostic procedure for all nodules.[13] They reserve imaging for nodules with doubtful FNB findings. Others maintain that the savings may be illusory.[10,14]

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Echography is widely used, but no echography pattern excludes or establishes a diagnosis of malignancy. Echography advocates claim that this method is useful for assisting in needle placement, especially in partially degenerated nodules.[3,15] However, proper FNB technique calls for punctures at many sites. The character of the aspirate will indicate whether cystic or solid tissue has been sampled. Echography is not cost effective.[10,16]

Diagnosis of thyroid nodules by needle biopsy dates from the 1930 report by Martin and Ellis.[17] They used a large needle aspiration technique. Reports from Cleveland[18] and Warsaw[19] confirmed the value of this technique. Subsequently, cutting needle biopsy specimens using Silverman or Tru-Cut needles were reported from several centers.[19,20,21] Acceptance of these methods was retarded by concern for malignant implants in the needle track[22,23] and because of a 1958 report of false negative biopsy findings in 26% of a series of surgically confirmed papillary carcinomas.[24] Ironically, the latter report came from the same hospital in which needle biopsy had been inaugurated 28 years earlier. Since FNB is a more simple and safe procedure, large needle biopsies are used less often. Accuracy of FNB can be comparable to that of the large needle procedures, and FNB is the principal biopsy method currently used.

FNB provides epithelial cells and tiny tissue fragments for cytologic evaluation. This technique was introduced by European workers in the 1940s.[25-35] North American physicians were slow to accept the concept that reliable diagnoses could be made from such small tissue samples, and were inhibited by concern for spreading cancer by the needle. An important handicap to increased use of FNB was a lack of pathologists trained to make FNB diagnoses. In the absence of illustrative reference material, the technique was learned by trial and error after a brief preceptorship with precocious colleagues in Toronto.[36]

Textbooks[2,37] and journal articles[38-42] now provide illustrations of both the FNB technique and the cytologic spectrum of thyroid disease. This literature has established FNB as a reliable diagnostic procedure in centers worldwide. Indeed, atlases of cytologic findings have been published recently in such diverse locations as the Netherlands[43] and Korea.[44] As Vickery[8] put it, it is "astonishing" that it took so long to convince physicians to use a diagnostic method of such value and safety for one of the most prevalent of medical problems.

However, the widespread introduction of FNB has inevitably led to frustration and disappointment for physicians who have been unable to duplicate the highly accurate results reported by FNB pioneers. Some researchers caution restraint in acceptance of the therapeutic implications of FNB diagnoses when clinical findings are contradictory, especially if experience is limited.[15,45] Some of these concerns reflect realistic limitations of FNB. Others are indicative of conceptual or technical deficiencies in the performance of the procedure. This review, after nine years' study of more than 4,000 ambulatory patients, should help others overcome such obstacles.

Conceptual Non-Problems

Some physicians find fault with FNB for invalid reasons, that is, "non-problems."

Implanting cancer in the needle track. There have only been two reports of implants of cancer in the needle track. One occurred in a patient with an extensive papillary carcinoma.[22] The second report was of a patient with metastatic renal carcinoma to the thyroid.[23] Two of our patients had implants of carcinoma in the wounds after surgery for thyroid cancer; neither had needle biopsy. Both lesions were excised under local anesthesia and presented no major problems. This concern should not deter physicians from using FNB.[46,47]

FNB does not detect occult carcinoma. Conventionally, nodules up to 1 to 1.5 cm in diameter have been termed occult. Many nodules of 0.5 to 1.5 cm in diameter are readily palpable, especially if favorably situated. Smaller, deeper nodules may be impalpable, or inaccessible for FNB. In neither case could FNB be done. The inability to use FNB in these instances should not negate its use when it can be helpful.[4,6,10]

When FNB is not possible for a palpable nodule, the decision to operate or observe will be based on conventional clinical criteria. For nonpalpable nodules the question of management is moot, because the nodule will not be detected. Granted, imaging or echography might be done for spurious reasons, and might detect an abnormality consistent with a nonpalpable nodule. However, those "lesions" do not require immediate treatment. Most clinicians limit diagnostic measures, and certainly surgical treatment, to patients with palpable nodules, believing that curable impalpable cancers will remain curable until they are palpable.

FNB may be hazardous. FNB might cause severe local hemorrhage[4,15] or damage to the recurrent nerve. We have experienced neither of these complications, even in patients taking anticoagulants. However, an occasional patient may have a local hematoma from piercing a superficial vessel.

Conceptual Problems

The principal objective of FNB is to reduce the amount of useless thyroid surgery that only removes benign nodules.[2,10] A second objective is to provide guidance for surgical planning to assure that the primary operation will be appropriate, neither unduly excessive, nor so inadequate that a secondary procedure will be needed.[48]

Impact of limited experience on results. It is widely held that FNB is cost effective by reducing unnecessary thyroid surgery.[5-7,10] However, Blum[15] questioned the validity of this concept, especially for those with limited experience. He warned that FNB diagnoses of benign thyroid nodules should not override clinical indications for surgery. If applicable to only a small minority of FNB-benign nodules, this would not vitiate the usefulness of FNB. However, regardless of FNB diagnoses, Blum and others[3,45] advised surgery for all nodules that did not respond to thyroxine therapy, and also for patients who have had upper body radiation therapy. Since, as Blum and others[45] observed, most nodules (benign or malignant) do not regress on thyroxine, nearly all nodules would be excised if this advice were followed.

FNB may be repeated when nodules fail to respond to thyroxine after one or two years, sooner for any nodule that seems to be enlarging.[5,47] If the FNB diagnosis is consistently benign, observation may safely be continued. Enlargement on thyroxine is more worrisome than no change, but more common causes than malignancy, in sum, are hemorrhagic degeneration, inflammatory disease, unappreciated autonomous function, and perhaps growth stimulating immunoglobulins.[49] In our experience, 97% of repeat FNB studies confirmed the original diagnoses, and excision of nodules with consistently benign FNB findings (usually to assuage continuing concern by the patient or attending physician) regularly confirmed the diagnosis of benign disease.

Radiation therapy to the upper body causes nodules of the thyroid. However, we and others have found that for any given nodule the chances of malignancy are no different than for nodule patients in general.[50,51] FNB is as useful for these nodules as for any others.[50,51]

Ramacciotti and associates[45] used indications for surgery like those of Blum; FNB did not improve on clinical selection. They operated on 50% of their patients; only 20% had a malignancy and there were 9% false negative diagnoses. These results are slightly worse than ours when we selected nodules for surgery by clinical methods,[52] before FNB. Ramacciotti and co-workers[45] warn that FNB lacks precision and should be used only as part of the overall clinical evaluation. Their FNB diagnoses were unreliable. However, they only studied 218 cases (111 underwent surgery), and performed only two aspirations per nodule. This was inadequate sampling in our opinion. It would seem prudent for physicians to defer judgment on FNB until a reasonable amount of experience has been obtained, at least several hundred patients. It is not that easy to learn the technique. Schwartz and colleagues[11] had 6.5% false negative diagnoses in a similarly small series. In our first 1,000 patients studied, the number we considered our basic training, we too used FNB to complement clinical-laboratory findings. Our subsequent experience justifies our current policy of placing primary reli-

TABLE I. FNB Diagnoses, Percent Malignancy, Diagnostic Category, and Recommended Initial Surgery for 501 Excised Thyroid Nodules

FNB diagnosis	No. of patients	% Malignant	Diagnostic category	Recommended initial surgery
Benign	68	1	Benign (1)	Observe; lobectomy*
Cellular adenoma	99	10	Possibly malignant (2)	Lobectomy, or observation for elderly or infirm
Hurthle cell adenoma	50	12		
Suspected carcinoma	102	35	Probably malignant (3)	Cancer operation, or lobectomy if patient prefers
Carcinoma	192	94		Cancer operation

* If surgery is done in spite of FNB diagnosis, it should be limited to lobectomy.
Adapted from Hamburger et al.[48]

ance for management decisions on FNB.[48] Other clinicians should have an easier time reaching an advanced level of expertise because of the availability of extensive illustrated teaching literature. Suen and Quenville,[7] on the basis of a study of 304 cases, increased malignancy in surgical specimens from 14% to 47%, while operating on only about 25% of their patients.

FNB cannot be equivalent in accuracy to surgical diagnoses. The surgical pathologist has the entire lesion and adjacent tissue to study as thoroughly as necessary to confirm or exclude malignancy. Granted, diagnoses sometimes are difficult, especially for follicular or Hurthle cell tumors.[4,53,54] When a diagnosis of malignancy is so difficult that experienced pathologists are uncertain, the problem is usually an encapsulated carcinoma versus an atypical (Hurthle cell) adenoma. However, regardless of the final diagnosis, since the lesion has been excised the patient has undoubtedly been cured.

Evaluating FNB specimens is more difficult. There are only cell clusters and tiny tissue fragments to study. From this limited material must be inferred not only the current architecture of the entire tumor, but also the probability of future malignant behavior if the lesion is not excised. It may be impossible to assure safety for nodules with FNB diagnoses of cellular (follicular) or Hurthle cell adenoma. These lesions, even if lacking microscopic features of malignancy when detected, might become more invasive in the future if they are not excised. For other lesions the diagnosis of malignancy, although strongly suspected, cannot be certain. Hence FNB diagnoses cannot always be as decisive as surgical diagnoses.

FNB data are used most often in the decision of whether to operate; but the data are also valuable in planning the extent of surgery after the decision to operate has been made.[48]

Use of FNB to decide whether to operate. Conventionally, FNB diagnoses are classified in categories that correspond to high, low, and negligible probability of malignancy. Table I lists the principal FNB diagnoses, the rate of malignancy at surgery for each, the biopsy diagnostic categories to which these FNB diagnoses are assigned, and the recommended surgical management for groups of FNB diagnoses.[48] Excluded are diagnoses of undifferentiated carcinoma, lymphoma of the thyroid, and metastatic carcinoma to the thyroid. These lesions are uncommon, may not require surgery, and operations when performed are usually only for palliation.

It is expected that FNB reduces unnecessary surgery, without any loss, or with an increase in the sensitivity of cancer detection. The philosophy underlying the assignment of specific FNB diagnoses to diagnostic categories may have a substantial impact on the usefulness of FNB. A comparison of our FNB categories[2] to those of the Mayo Clinic[55] is illustrative (Table II). Both centers classify FNB diagnoses into three categories, but there are important differences in the composition of those categories. We include in our Probably Malignant category lesions for which malignancy is strongly suspected, and

TABLE II. Comparison of Our FNB Diagnostic Categories With Those of the Mayo Clinic

Hamburger et al*			Mayo Clinic†		
Diagnostic category	FNB diagnoses included	% of FNB diagnoses	Diagnostic category	FNB diagnoses included	% of FNB diagnoses
Benign (1)	Nodular goiter; Hashimoto's thyroiditis	67	Benign (1)	—	78
Possibly malignant (2)	Cellular or Hurthle cell adenomas	18	Suspicious (2)	All possibly malignant for which FNB findings were not conclusive	17
Probably malignant (3)	Suspected or definite malignancy	15	Malignant (3)	Definite malignancy	5

* Data adapted from Hamburger et al.[2]
† Data adapted from Gharib et al.[55]

TABLE III. Relative Accuracy of Clinical and FNB Diagnoses

	Hamburger et al*		Mayo Clinic†	
	Clinical diagnoses	FNB diagnoses	Clinical diagnoses	FNB diagnoses
Number of cases	1,094	2,500	64	1,970‡
Number of operations for Category 2 and 3 FNB diagnoses (%)	523 (48)	433 (17)	41 (64)	351 (18)
Specificity for malignancy of Category 3 FNB diagnoses (%)	111/333 (33)	218/284 (77)	—	98/98 (100)
Specificity for malignancy of Category 2 FNB diagnoses (%)	15/190 (8)	16/149 (11)	—	60/233 (24)
Sensitivity of Category 3 FNB diagnoses (%)	111/126 (88)	218/234 (92)	—	98/158 (62)
Number of cancers detected for Category 2 and 3 FNB diagnoses	126	234	6	158
Number of cancers/100 operations for Category 2 and 3 FNB diagnoses	24.1	54	14.6	45

* Adapted from [52] and [48].
† Adapted from [5] and [55].
‡ Includes multinodular goiter and diffuse goiter, as well as discrete nodule.

those lesions that are clearly malignant. In the Mayo Clinic study only definite malignancies are included in the Malignant category. Other highly suspicious lesions are assigned to the intermediate Suspicious category.

Table III compares the accuracy of nodule diagnosis based on conventional methods used prior to FNB, with that achieved with FNB by us and by the Mayo Clinic. Some of our patients also had large needle biopsies, but they were used for fewer patients recently[48] because of our increased confidence in FNB.

In both centers FNB was more accurate than clinical methods. FNB Category 2 and 3 diagnoses led to surgery for similar proportions of patients, 17% and 18%. However, only 77% of our Category 3 nodules were malignant; all of their Category 3 nodules were malignant. Hence the specificity of their FNB Category 3 diagnosis was much higher than ours. However, the sensitivity for malignancy for our Category 3 diagnoses was 92%, as compared to 62% for the Mayo Clinic. This difference reflects the enrichment of their Suspicious category with cancers for which FNB findings were not absolutely diagnostic of malignancy. Thus their Suspicious group had 24% malignancy, some high grade including an anaplastic carcinoma. Our Possibly Malignant group had only 11% malignancy, and those were of the mini-invasive type. Finally, the cancer rate in patients operated on for FNB Category 2 or 3 diagnoses at the Mayo Clinic was significantly less than for ours (by chi square analysis, $P < 0.02$).

In the Mayo Clinic study, surgery was advised for all of their Suspicious (Category 2) nodules, although 76% were benign. Thus this diagnosis had little clinical utility. They might as well have had only two categories, Surgery and Observe. Our Category 2 diagnosis is more useful because it implies that observation may be safe whenever advanced age or infirmity increases surgical risks.

Hence the differences in sensitivity and specificity of data from the two centers that lead to different management recommendations reflect philosophic differences, rather than differences in experience. Perhaps their diagnostic categories were designed to cater to pathologists' concerns for overdiagnosis of malignancy. This is consistent with sound pathology practice for nodules that have been excised. Overdiagnosis of malignancy may lead to unnecessary, costly, and sometimes hazardous postoperative treatment. However, this concern is irrelevant in the determination of which nodules should be excised.

Our biopsy categories catered to needs of clinicians. Clinicians neither required nor expected that test data used to select thyroid nodules for surgery or observation would be as specific as surgical diagnoses. Clinicians use FNB to improve upon the relative inaccuracy of those conventional clinical methods that led to false positive diagnoses of possible malignancy for 75% of nodules for which surgery was advised, and 67% of the most suspicious lesions,[52] 86% for the Mayo Clinic.[5] Thus, clinicians hoped that FNB would reduce the amount of unnecessary surgery, while not increasing the number of false negative diagnoses. This objective was well served by Category 3 diagnoses that were highly sensitive, for which surgery was routinely advised. A Category 2 diagnosis with a low probability of malignancy, and virtually no risk of a high grade cancer, was useful because these patients might be observed if elderly or infirm. Although each center must establish criteria for FNB diagnostic categories that address the principal concerns of their constituent physicians, we think our approach, designed by and for clinicians, will best serve the needs of most physicians who deal with patients with thyroid nodules.

Use of FNB in surgical planning. The unreliability of frozen section (FS) diagnoses for thyroid nodules is well known. This method is most likely not to be helpful when help is most needed (eg, for follicular and Hurthle cell lesions). Most pathologists will not even try to rule out malignancy on those lesions by FS. On occasion a diagnosis of malignancy may be made if the microscopic findings are incontrovertible, but this is the exception. Ashcraft and Van Herle[4] recently documented the frequency of false negative FS diagnoses. Goldfarb and associates[10] and Esselstyn and colleagues[9] found needle biopsy more reliable than FS. Rosen and Maitland[56] provided limited data in support of this concept. Our study of 359 patients who had FS after needle biopsy showed that FS diagnoses were never more reliable, and usually were less reliable than biopsy diagnoses.[48]

When the surgical procedure is planned preoperatively on the basis of FNB findings, rather than on the intraoperative FS findings, the plan may be discussed with the patient, explaining the limitations in accuracy of FNB and the risks of inadequate versus overly aggressive surgery in order to obtain informed consent for the surgical plan.

We translate our FNB diagnoses into surgical management recommendations as shown in Table I.[48] For most FNB diagnoses of frank malignancy (confirmed 94%) or suspected malignancy (confirmed 35%), we advise primary cancer operations (usually total or near total thyroidectomy, depending on the surgeon's preference). Involved lymph nodes are excised as indicated. For differentiated carcinomas smaller than 1.5 to 2 cm in diameter, without evidence of metastases or multicentricity, the safer lobectomy-isthmectomy will nearly always be adequate treatment.[57-59] When surgical planning is based on FNB data, more extensive surgery than necessary may be done for the minority of patients who have had false positive FNB diagnoses of malignancy. However, when the probabilities of cancer are high, to most patients the risks of a cancer operation by a qualified thyroid surgeon are less threatening than the prospects for a second surgical procedure, if an inadequate primary resection was performed. If the patient prefers a lesser primary operation, it may be done without fear of retrospective recrimination. For nodules with FNB diagnoses of suspected carcinoma, prospective patient discussion is especially important. Although the risk of cancer is relatively high (35%), most of these nodules are benign. Appreciation by the patient of the uncertainty of the final diagnosis is essential to agreement on the plan for the primary operation. We encourage a cancer operation, but again accede to the wishes of patients who request less extensive procedures.

Finally, for low risk nodules, when a decision to operate is made, we advise lobectomy (with or without the excision of the isthmus), confident that 90% or more of these lesions are benign, and that the malignancies are nearly always of the mini-invasive type. If metastases are discovered at surgery, the procedure is expanded appropriately.

Reliable FNB diagnoses permit most frozen section examinations to be eliminated. The exceptions are nodules for which FNB cannot be done, those for which FNB produces unsatisfactory specimens, nodules discovered during the operation that had not been appreciated preoperatively, and finally for lymph nodes detected at surgery that may harbor metastases in patients with FNB diagnoses that suggested low risk lesions.[48]

Technical Difficulties With FNB

Technical problems relate to the method for securing and preparing the specimen, and to the interpretation of the specimen. With regard to interpretation, FNB diagnoses may be falsely negative or falsely positive. Neither error may be completely eliminated. Good technique and awareness of factors contributing to interpretative errors can minimize FNB failures.

Anesthesia. We use local anesthesia because many punctures are made in order to assure adequate sampling. Some argue that anesthesia is unnecessary,[3,5-7] and that the injected fluid may obscure margins of the nodule, making needle placement more difficult. Most patients are apprehensive about FNB. Without anesthesia there is greater danger of patient movement or muscular contraction that may make the biopsy more difficult, and possibly more hazardous. With gentle massage the injected fluid promptly disperses in the subcutaneous tissue, and the anatomy of the nodule is not obscured.

Syringe holder. Some workers use a mechanical syringe holder to permit continuous palpation of the nodule during FNB.[6,47] Otherwise, after the needle has been inserted into the nodule, one must use the other hand to hold the barrel of the syringe to withdraw the plunger and apply negative pressure. However, immediately thereafter the opposite hand is free to fix the nodule throughout the balance of the biopsy procedure. We found the syringe holder awkward. It removes the hand holding the biopsy syringe and needle farther from the nodule, with a loss of the sense of touch that is helpful in determining whether the needle is within the nodule.

Needle size. We use a 25 gauge, 1½ inch disposable needle in most cases. For the very dense nodule from which it is difficult to obtain a specimen, a 22 gauge needle may be used. However, the routine use of 21 to 22 gauge needles, as some advise,[11,47] will produce excessively dilute specimens consisting mostly of blood or degeneration fluid. One center attempted to solve this problem by filtering the overly dilute specimen through a Millipore filter,[47] unnecessarily complicating the procedure. The finer 25 gauge needle prevents the problem most of the time. On the contrary, some workers use needles as fine as 27 gauge.[3] They are so flexible that it is more difficult to be certain of the needle tip location.

Needle placement. Little has been written about where to place the needle for FNB. For small nodules there is not much choice. However, for larger nodules the center of the nodule—where degeneration is most likely and follicular cells are less numerous—should be avoided. Instead FNB should be performed circumferentially at the periphery.

Adequate sampling. We have consistently advocated many samplings, at first four, and currently six and more, depending on the character of the specimens. Scanty or bloody specimens are not discarded but must be recognized as less promising, and additional samples should be taken to compensate for them. Most of the false negative diagnoses in our first 1,000 cases were attributed to inadequate samples. Others have been content with one or two[6,11,45] or several aspirates.[7,55] Perhaps less aspirates are performed because local anesthesia is not used and the patients object to many punctures. Thus one technical lapse may contribute to another.

Tissue disruption. Some disruption of the tissue is needed to obtain a specimen. Sometimes the tissue is so loosely organized that suction is enough. If suction alone does not produce a specimen, and usually it will not, the most efficient maneuver is that described by Lowhagen and associates.[6] Suction is maintained and the needle is moved in and out within the nodule through a depth of 1 to 2 mm (depending on nodule size). This maneuver is repeated as often as necessary to secure the specimen. An alternative maneuver that may be used is rotation of the needle within the nodule while suction is maintained. The sharp bevel of the needle will sever tissue fragments that

are aspirated into the needle. This technique will produce excess bleeding for most nodules. It should only be used for very dense nodules.

Extracting the specimen. The biopsy maneuver is terminated when fluid appears in the hub of the needle. The plastic hubs of disposable needles are ideal to visualize specimens. Once the specimen enters the hub of the needle the suction is released, and only then is the needle withdrawn. If suction is not released before the needle is withdrawn, the specimen will be aspirated into the syringe and effectively lost. After withdrawal the needle is detached from the syringe, air aspirated into the syringe, and ejected through the needle to flush the specimen onto a slide for smearing. Immediate fixation is essential to prevent the air drying that would render Papanicolaou smears difficult to interpret.

Staining. Many Europeans prefer air dried smears stained with Giemsa stain.[6,60] However, Papanicolaou staining produces greater clarity of nuclear detail. Virtually all US cytopathologists use Papanicolaou staining because they depend on nuclear detail for diagnosis.

False Negative Errors

Adequacy of sampling. The principal cause of erroneous diagnoses of benign disease is inadequate sampling. Although a few clusters of malignant cells are enough to diagnose cancer, a similar number of benign cells does not exclude cancer. Excluding malignancy requires more stringent criteria. Malignant cells come only from a malignant nodule. Every thyroid gland has benign cells in normal thyroid tissue adjacent to the nodule. Also, even though malignant thyroid nodules are malignant throughout, cells from some portions of a malignancy may be more obviously malignant than others. Many aspirations from different portions of the nodule assure adequate sampling. Making many smears from a single aspirate is an unacceptable alternative. It is not the number of smears that is important, but rather the number of nodule sites sampled. Also, aspirates voluminous enough to prepare several smears probably are too diluted with blood or degeneration fluid to be useful.

The pathologist should report not only the diagnosis, but also the number of slides that contained epithelial cells and the number of cell clusters on each slide. We require six or more cell clusters on at least two slides, all of which are benign, before accepting a FNB diagnosis of benign. Fewer cell clusters on more slides might also be acceptable. If the specimens contain inadequate cellular material, the pathologist should report that the sampling was inadequate to exclude malignancy, along with a description of the cells that were observed. The physician who evaluated the patient and performed the biopsy may then decide whether that number of cells might be adequate for the size and type of lesion biopsied, or whether a repeat biopsy should be done to obtain more cellular material. The larger the nodule, the more cells required, and vice versa. No amount of amorphous or fibrous material by FNB is of any diagnostic value. Malignant nodules may degenerate, and have extensive areas of fibrosis.

Multiple nodules. When there is more than one nodule, all accessible nodules should be biopsied. The findings on the largest or firmest nodule need not be representative of those for the other nodules.

Cystic lesions. A study of cyst fluid cannot exclude cancer.[3,61] Failure to find thyroid epithelial cells (the usual finding), or the finding of a few benign cells or macrophages has no importance. The discovery of clearly malignant cells is useful, but uncommon. It is possible to biopsy the capsule of cystic lesions using larger needles. However, these biopsies are useful only if the specimens are positive. Only a small portion of the capsule is sampled by this technique. FNB may be tried on a solid residual after cyst aspiration. The specimens more often are acellular or contain few cell clusters because of dilution with residual cyst fluid. If FNB is not possible and the cyst recurs after several aspirations, and in spite of the instillation of tetracycline,[62] a risk of cancer of 10 to 20% must be appreciated.[4,61,63]

Follow-up of FNB benign diagnoses. After an FNB specimen is found to be benign, further follow-up study is needed. Young patients may be treated with thyroid hormone in the absence of autonomous function. Enlarging nodules, or those failing to regress after one to two years' treatment with thyroid hormone, should have a repeat FNB, or a large needle biopsy when practical. It is uncommon for the findings on a second FNB to reverse a benign diagnosis made on a previous FNB. However, this is possible and more common when the physicians are still gaining basic experience with FNB performance or interpretation. Growth of a nodule in spite of treatment with thyroxine may be caused by several processes, but only infrequently by malignancy.

Misleading diagnosis of Hashimoto's thyroiditis. A diagnosis by FNB of Hashimoto's thyroiditis may be correct but irrelevant for the lesion of concern. With Hashimoto's thyroiditis there may be papillary carcinoma, Hurthle cell tumors, or lymphoma.[39] All are uncommon, but FNB is not ordinarily performed in patients with Hashimoto's thyroiditis unless there is a localized mass, enlargement of the goiter in spite of treatment with thyroxine, or a large hypofunctional area on a thyroid image.[64] With these indications one should be certain that criteria for adequate sampling have been fulfilled.

Calcified nodules. Calcified nodules may be malignant. If one strikes calcium while performing a FNB, the procedure should not be abandoned on the assumption that the nodule is benign. Insertion of the needle between calcium deposits may permit the diagnosis of papillary carcinoma.[65]

False negative diagnoses by surgical pathologists. Another source of confusion is a discrepancy between a correct FNB diagnosis of malignancy and an erroneous diagnosis of benign disease on the surgical specimen.[48] Pathologists providing FNB diagnoses usually have special interest and expertise in thyroid pathology. However, the subsequent operations may be done in other institutions in which the surgical specimens are studied by pathologists with lesser experience.[48] This is more common outside of large medical centers. Some of our cases were so difficult that conflicting diagnoses on the surgical specimens were obtained even from different nationally recognized authorities in thyroid pathology. However, most of the errors were corrected by local review and reevaluation by the original surgical pathologist. On occasion not

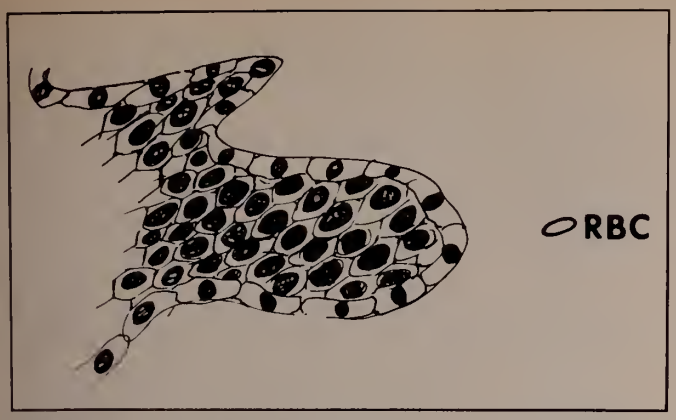

FIGURE 1. A typical honeycomb; diagrammatic. Nuclei are uniform, all oriented in the same direction, and cytoplasmic borders are well defined. Note relative size of nuclei to a red blood cell (RBC). Reprinted from Hamburger et al,[2] with permission.

enough sections are prepared, especially in follicular or Hurthle cell tumors. For these tumors very extensive study is necessary if isolated foci of capsular or vascular invasion are to be discovered. In other cases evidence of malignancy, although present, was overlooked. Hence, with conflicting biopsy and surgical findings, further study of the specimens and slides, or consultation by pathologists with special interest in thyroid disease, is indicated.

False Positive Errors

False positive FNB diagnoses of malignancy, as already noted, are less worrisome to clinicians as long as FNB reduces unnecessary surgery by 50% or more. To avoid what most clinicians view as the greater peril (ie, failing to diagnose cancer), a substantial number of false positive FNB diagnoses are unavoidable.[6,7] Nevertheless, some false positive FNB diagnoses may be eliminated.

Differentiation of papillary fronds of nodular goiter from papillary carcinoma. In nodular goiter papillary fronds have the honeycomb appearance typical of benign disease (Fig 1). Nuclei are uniform in size and shape, constant in polarity, and the cell borders are sharply defined. In papillary carcinoma there is a monolayered sheet of cells with indistinct cell borders, nuclear pleomorphism, loss of polarity, and cytoplasmic inclusions or "nuclear holes" (Fig 2). In papillary carcinoma multinucleated giant cells are common, and psammoma bodies may be seen. Inspissated colloid within a small follicle may superficially resemble a psammoma body, but the typical concentric lamellations are lacking.[38]

Differentiation of Hurthle cells of Hashimoto's thyroiditis or nodular goiter from those of Hurthle cell tumors. In nodular goiter and Hashimoto's thyroiditis the honeycomb pattern is common. Nuclei are not pleomorphic and may be pyknotic. Macronucleoli are lacking, and there are admixtures of normal follicular epithelia. There are varying numbers of lymphocytes in the background, as well as clinical and laboratory evidence of Hashimoto's thyroiditis. In Hurthle cell tumors the monomorphic pattern of one cell type is striking. Nuclei are eccentric and contain prominent cherry-red macronucleoli. Nuclear pleomorphism is prominent and binucleation is common. The cells are often isolated or in loosely cohesive groups.[40]

Differentiation of benign follicular lesions from follicular carcinoma. The difficulty in making this differentiation by FNB is well known [53-55] and many physicians do not even attempt to make it.[3,6,7,10,11] However, findings of malignancy may be obvious, and the diagnosis of follicular carcinoma may be either made or suspected about 70% of the time.[42] Most of the remaining follicular carcinomas will have FNB findings of cellular adenoma. Only 1 to 2% of the more well-differentiated follicular carcinomas will be determined on FNB as nodular goiter.[42] Perhaps the most useful finding is the increased nuclear size of follicular carcinomas,[42] as shown in Figure 3. Nuclear pleomorphism, and the presence of micro and macronucleoli are helpful signs of malignancy, but well-differentiated carcinomas usually lack these findings. An irregular follicular pattern, and a syncytial appearance with crowded and overlapped nuclei suggests possible malignancy. The hypercellular nodular goiter is identified by the typical honeycomb appearance, or a pattern of regular follicles with uniform small nuclei.[42]

Spindle cells. It is important to differentiate spindle shaped stromal cells from the spindle cells of undifferentiated carcinoma. Stromal cells are seen in isolated cohesive groups. The nuclei have a fine chromatin pattern, and micronuclei may be seen. A background of normal follicular epithelium is typical. Spindle cells of undifferentiated carcinoma are noncohesive, pleomorphic, and numerous.[37]

Table IV summarizes contrasting features that serve to differentiate most malignant lesions from benign counterparts with a superficial resemblance.

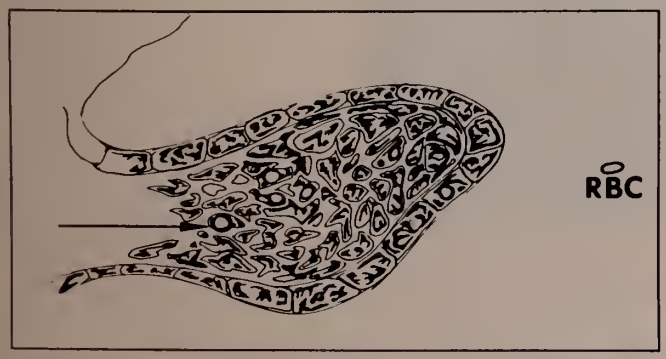

FIGURE 2. A papillary frond of papillary carcinoma exhibiting loss of polarity of nuclei of various sizes and shapes and a nuclear hole; diagrammatic. Reprinted from Hamburger et al,[2] with permission.

FIGURE 3. Follicular carcinoma; diagrammatic. Note the large nuclei (compared to a red blood cell) with prominent nucleoli. The nuclei vary in size and shape and have coarsely granular chromatin. Reprinted from Hamburger et al,[2] with permission.

TABLE IV. FNB Findings Useful to Differentiate Benign From Malignant Nodules

Findings	Benign pattern	Malignant pattern
Appearance of tissue fragment	Honeycomb with uniform cells, sharply defined cell borders, and retained nuclear polarity	Heaped up cells with syncytial pattern, loss of nuclear polarity, and nuclear atypia
Uniformity of cell type	Atypical or Hurthle cells are associated with predominantly normal follicular epithelia or lymphocytes if multiple samples are taken	Monomorphic pattern of atypical or Hurthle cells
Cohesiveness of cells	Typically cohesive	Isolated or loosely cohesive

Summary

The objectives of FNB and surgical pathology diagnoses for thyroid nodules are fundamentally different. Surgical diagnoses indicate whether excised nodules are benign or malignant. However, the principal objective of FNB is to prevent unnecessary thyroid surgery by identifying nodules that need not be excised.

FNB can identify two groups of nodules for which surgery may be avoided for nearly all, or at least some patients. For the first group (our Category 1), the risk of malignancy is virtually nonexistant. For the second group (our Category 2), low grade malignancy is possible, but the incidence is only about 10%. Accordingly, observation might be advised when advanced age or infirmity increases the risk of surgery, or the expected survival of the patient would not be enough to permit the full potential, if any, for malignant behavior.

FNB also provides guidance for surgical planning after a decision to operate has been made. For patients with low risk lesions, limited operations could be planned. Those with higher risk lesions could have cancer operations. With experience, FNB diagnoses may replace frozen section findings in surgical planning. The goal is to select a primary operation that is adequate, but not unnecessarily extensive for the disease. When surgical planning is based on FNB data rather than frozen section, the extent of the operation proposed may be discussed with the patient preoperatively. This assures informed consent and reduces the potential for retrospective patient recrimination if the primary operation proves not to be ideal. It also provides the opportunity to select a surgeon with the requisite competence, especially in the case of thyroid cancer.

To achieve these objectives with FNB requires experience and good technique. A study of published didactic and illustrative material will hasten the acquisition of adequate experience. The most important technical principle is adequate sampling.

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PICTURE OF THE MONTH

Sundown over the Niger River, Niamey, Niger Republic (Pascal James Imperato, MD). Taken with an Asahi Pentax Spotmatic with a Super Takumar 1:1.4/50 mm lens, f. 5.6, 1/125 second.

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Qualitative and ethical issues in quantitative clinical decision making

SAUL V. MOROFF, MD

A painful irony pervades western medicine today. As diagnostic tests have become increasingly sophisticated, costly, and often hazardous, physicians have become more troubled by the imperfect nature of these tests. Gold standards in diagnosis are few; only the rare positive test result consistently guarantees the presence of a disease, and negative results often fail to assure its absence.[1] It seems to the worried physician that the more sensitive and specific a test, the greater its cost is likely to be in terms of money, discomfort, inconvenience, and physical danger. In therapeutics, impressive progress in treating serious illness has advanced side by side with new iatrogenic diseases. Patients' expectations of success are high, and they are both surprised and disappointed when treatment is ineffective or even leads to a state worse than that in which they began.

Early in the 20th century, physicians began losing their image as compassionate healers at the same time that they were starting to earn a reputation as clinician-scientists. The stethoscope, microscope, and the x-ray machine made diagnosis more certain; observant physicians were sorting out one pathologic entity from another and were beginning to bring order out of the chaos of fevers, inflammations, and catarrhs. Prognosis, a proud skill of physicians since the time of Hippocrates, began to take on greater validity. However, most treatments remained symptomatic at best, and irrelevant or harmful at worst. Physicians could not do much more for seriously ill patients than palliate their symptoms while their affliction worsened. Uncertainty in the outcome of therapeutic intervention was taken for granted, and patients' interest in diagnosis was limited to its influence on prognosis.

The advent of modern medicine, beginning with the development of safe surgery and effective antibiotics, led to a new confidence in medical care that was, for a time, high among physicians and patients alike. Over the past decade, this confidence has been shaken, partly as a result of the heights to which it had risen, partly as a manifestation of society's ongoing loss of reverence for professionals as authority figures, and partly because of the growing understanding by physicians themselves of the limits of their knowledge. Uncertainty has re-emerged as a visible presence in the practice of medicine; the irony lies in the observation that although there is much less uncertainty in medicine today than in the premodern era, its very existence causes physicians more distress than their predecessors experienced two generations ago. The more physicians know, the more they are troubled by what they do not know.

The anxiety of physicians in the face of this uncertainty has fueled the development of two important sets of medical decision making tools. The first, clinical epidemiology, encompasses a variety of techniques aimed at the explicit acknowledgment and quantification of uncertainty in diagnosis and prognosis, and a logical manipulation of what is known in an effort to reduce uncertainty to a more tolerable level. The second, decision analysis, including analyses of utility, cost-benefit, and cost-effectiveness, employs processes intended to achieve the best possible average outcomes of medical decisions, despite an inability to know in any given instance whether they will result in benefit, harm, or neither.

DECISIONS IN DIAGNOSIS

Quantitative decision making in diagnosis has won many adherents among physicians. Though large gaps persist in knowledge of the qualities of certain diagnostic tests, few physicians question the principles involved in using them to alter the probability of disease in an individual patient. There is an elegance in the use of Bayesian analysis, 2 × 2 tables, and flow diagrams that convinces the novice and wins over the cynic. Once the physician accepts the premise that even his most treasured tests may sometimes be wrong, he is willing to use whatever techniques he can to be right as often as possible. To be sure, skeptics abound who spurn the diagnostic techniques of clinical epidemiology and continue to seek truth through

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intuition and volume. Uncertainty in diagnosis is increasingly recognized as a measurable entity that may be steadily eroded, and not as a specter to be intimidated by or ignored in the hope that it will disappear.

In customary practice, clinical epidemiology is more a concern of physicians than of patients. With few exceptions, the latter seek relief more than knowledge when they consult a physician. Patients desire reassurance from fear, alleviation of symptoms, lessening of disability, and cure of disease. Pathophysiologic diagnosis—the scientific identification and labelling of anatomic and biochemical disease—is less important to patients than to clinicians, for whom it has become a necessary means to the end of rational therapy. In general, patients take little interest in the choice of diagnostic tests, and less in their interpretations. In a patient with atypical chest pain, the decision whether to follow up a weakly positive exercise stress test by ordering a thallium myocardial perfusion study or to proceed directly to coronary angiography is usually left to the physician. It is an arithmetical problem, one in which the physician seeks to minimize his own uncertainty; the patient is often unaware of that uncertainty and uninvolved in the process of diagnosis. The 50-year-old man with high blood pressure cares more that his doctor will lower the blood pressure and keep him well than whether his problem is a manifestation of an aldosterone-secreting adenoma or of ordinary essential hypertension. In current practice, most diagnostic decisions continue to be made by physicians.

There are circumstances, however, where the choice of tests intrudes upon the patient's consciousness as well as the physician's, and raises concerns that numbers alone cannot resolve. One of these circumstances is the cost of the test in dollars, time, inconvenience, and physical and psychologic distress. For some patients, high financial cost alone is sufficient cause for rejection of a test; indeed, for the uninsured patient without adequate funds, there may be no choice but to forego the study. For others, the cost of the test must be weighed, by some more or less explicit calculus, against the benefits that it promises. Physicians occasionally behave as if they were pure scholars; they value knowledge highly for its own sake and seek to know as much as possible about their patients, regardless of what may be done with that knowledge. On the other hand, patients are more likely to measure their need to know in terms of the effect of additional information on their physical and emotional health. Thus, the greater the potential benefit of a test—that is, the more likely it is to lead to effective therapy—the more willing the patient is to undergo it.

For the physician of a young woman with an acute onset of low back pain, a computerized tomographic study of the lumbosacral spine may substantially reduce the diagnostic uncertainty between undifferentiated low back syndrome and herniated nucleus pulposus; the information that the test may provide is substantial. If the patient is told that her initial treatment will consist of bed rest, aspirin, and diazepam regardless of the diagnosis, and told in addition that the test will yield her 200 millirad of ovarian irradiation and a bill of $600, its merits may well be less impressive to her. Similarly, though physicians argue the relative accuracy of endoscopy versus upper gastrointestinal radiography in the evaluation of patients with dyspepsia, the need for either method is questioned if the initial treatment for any of the major diagnostic considerations will consist of antacids and a period of watchful waiting.[2,3] A lumbar puncture, however unpleasant, is "worth it" to the patient with probable bacterial meningitis for whom an organism must be identified and an antibiotic regimen selected; it may not be worth the pain or even the minute risk of prolonged disability for a patient with a positive serum VDRL test and a normal neurologic examination. In this instance, the benefits of exact diagnosis are less certain, and the patient might prefer that the physician prescribe an adequate course of penicillin without studying the spinal fluid.[4]

Decisions Regarding Prognosis

Diagnostic tests serve purposes other than to determine treatment, and it is here that nonquantitative considerations become even more important. The desire to know one's prognosis in a given state in the absence of effective treatment is subject to distinct patient preference. For someone who has recovered from an attack of acute optic neuritis, the presence of oligoclonal bands in the spinal fluid may make the diagnosis of multiple sclerosis almost certain.[5] However, is that diagnosis one that the patient necessarily wants to know or is it one that the physician is obligated to discover? The once-sexually active homosexual man, now celibate, may have a desperate emotional need to learn the result of a test for the presence of HTLV-III/LAV antibody, or he may just as strongly desire not to know. The likelihood that he will develop the acquired immune deficiency syndrome (AIDS) is independent of whether or not the test is done. Some patients will feel that they cannot live without that knowledge, and others that they cannot live with it. Either choice must be respected by the physician. In the absence of overriding public health considerations, the physician may only inform the patient of the diagnostic, prognostic, and therapeutic implications of doing the test and of the test's specificity and sensitivity; the patient must decide whether it is to be done at all. Bayesian analysis informs us what we can expect to learn from a test; it cannot predict or measure the value of the knowledge gained. Here the conflicting goals between physician and patient become dramatically manifest. Most physicians are uncomfortable with the realization that knowledge may occasionally produce more harm than good; patients are often convinced of it, though sometimes after the fact.

Tests as Therapy

Tests serve therapeutic as well as diagnostic and prognostic purposes. What physician has not cared for a patient whose chest pains disappeared after a normal stress test, or whose backaches became more bearable when he learned that his lumbar spine was normal on radiographic examination? The importance to the patient of the upper gastrointestinal x-ray series[6] and the electrocardiogram[7] has been demonstrated in recent studies. The phenomenon of placebo therapy is well known, but the therapeutic efficacy of a test is seldom consciously considered. To the physician, a normal test result may lower the probability of a particular disease from 2% to 0.2%, and this modest

decrease may well be regarded as diagnostically unimportant. Yet the worth of that tenfold reduction in disease probability in terms of reassurance to the patient may be incalculable.

Therapeutic Decision Making

The other major use of quantitative techniques in decision making revolves around the strategy of decision analysis, in which management alternatives are made explicit, probabilities assigned to chance events, and numeric values given to potential outcomes.[8] Decision analysis has been shown to be of enormous benefit in clarifying complex and difficult dilemmas. It illuminates the responsibility of the physician to provide medical information and that of the patient, if willing, to measure expected outcomes according to his or her unique goals. Examples of the usefulness of decision analysis abound in the medical literature: the choice among alternative therapies in malignant disease[9]; the diagnosis and treatment of thyroid nodules[10]; and the optimal approach to the patient with dysuria.[11] The major technical difficulties of decision analysis are apparent to proponents and detractors alike. Estimates of probabilities are too often based on inadequate data; the proper assignment of numbers to outcomes, even when patients can arrange those outcomes in rank order of preference, is frustrating and difficult. Decision analysts and psychologists continue to wrestle with the negative worth of death measured against a life of pain, mutilation, or dysfunction, and attempt to compare the utilities of less-than-optimal outcomes against each other. Quality of life distinctions produce discomfort in physicians traditionally charged with the duty to extend life; they are more immediate and meaningful, but no easier to quantitate for patients.

These barriers to effective decision analysis are formidable but not insurmountable. The expansion of information makes probability estimates more firm with each passing year, and techniques of utility analysis offer at least the hope that physicians and patients will learn to translate outcomes into measurable and thus comparable units.

Even those who concede that resolution of these difficulties is possible, however, continue to view decision analysis with discomfort. The reason for this unease may lie in the essential premise of decision analysis. As it is customarily employed, decision analysis seeks to determine the maximum expected utility for a given choice of action. It views the individual patient as if he or she were cloned over and over. For 1,000 identical patients in exactly the same circumstances, decision analysts can determine that more patients will benefit from action A than from action B. Since decision analysis cannot predict what will surely happen but merely what will happen more often than not, because of the very uncertainty that dictates its use, it adheres (in philosophical terms) to a pure utilitarian approach. That philosophy is guided by the principle that seeks the attainment of the greatest good for the greatest number, and decision analysis correspondingly yields a recommendation based on the probability of the best outcome on average. Of course, the analysis need not necessarily be couched in utilitarian terms; rather than point to the best average or expected utility, it may be used to select that choice that will maximize the likelihood of the best possible outcome (in the eyes of the patient) or minimize the probability of the worst possible outcome.

A profound philosophic conflict lies at the root of physician resistance to decision analysis. Physicians, by their training and philosophy, are not driven by utilitarianism but by an ethic of duty. Two principles hold strong and sometimes contesting positions among physicians. One is that of nonmaleficence[12]; it is the duty of the physician not to harm patients, as expressed in the familiar phrase *primum non nocere*. Nonmaleficence is the principle that warns the physician against causing harm to the patient, even in the pursuit of best serving the patient's welfare. Rather than judging a death resulting from treatment and a death from disease to be equally undesirable, as utilitarianism would do, it regards the iatrogenic death as consistently the worse of the two. Adherence to the duty of nonmaleficence leads physicians to bend their efforts towards the avoidance of errors of commission. Indeed, since virtually all methods of treatment are potentially harmful, the physician committed solely to the avoidance of harm would be paralyzed; he could not bring himself to employ any therapeutic modality because of concern that the action might prove detrimental to the patient.

The second principle, equally compelling in the belief of most physicians, is that of beneficence,[12] the duty to strive always to do good for the patient. To the physician driven by beneficence, it is the error of omission that is unforgivable. No consideration can absolve the physician of the obligation to pursue every therapeutic option, however unlikely of success, if it offers even a small chance to help the patient.

Stereotypically, these sometimes conflicting principles might be regarded as informing two kinds of physicians: the activist who will take any risk that might benefit the patient, and the contemplative physician more willing to lose a patient to disease than to be the source, however unintended, of direct harm.

In an insightful essay, Feinstein[13] uses the phrase "chagrin factor" to explain physicians' resistance to classical decision analysis. Physicians and patients both, he argues, will pass up the best average outcome in order to avoid the choice that leads to the least desirable outcome and thus produces the greatest degree of chagrin. In psychologic terms, they are risk avoiders rather than risk seekers. Obviously, a risk too painful for one participant to face may be well worth assuming in the opinion of the other.

Kassirer[14] has written of these differing attitudes toward opposing risks in everyday medical decision making; too often the physician and patient regard risks that are acceptable to the other as intolerable and unacceptable to themselves. Whereas physicians tend to weigh heavily the very small probability of a bad outcome, patients are more willing to take that risk if it is coupled with a highly likely chance of a good outcome. Further, physicians tend to see outcomes in black and white terms: cure versus no cure, success against failure, life or death. Patients are more likely to be concerned with quality of life considerations; they see outcomes in varying shades of gray.

The treatment of mild hypertension provides an excellent example of medical decision making. Physicians know, or believe they know, that lowering the blood pres-

sure from 150/95 mm Hg to 130/80 mm Hg will, in a small but definite number of patients, prevent the later development of stroke. To avoid that outcome in a few, they are willing to prescribe medication to all patients. For each patient saved from stroke at some future time, many patients who would not have become ill even if left untreated will experience the usually mild, but nonetheless troubling side effects of therapy.

Decision analysts can assign values to these outcomes, but the validity of the numbers is doubtful. How much cumulative fatigue in patients on beta adrenergic blockers equals or outweighs, in utilitarian terms, the cost of one stroke? How does a patient compare the near certainty of drug-induced symptoms, or the daily reminder of disease that each pill-taking evokes, with a reduction of the small probability of serious harm at some future date from uncorrected hypertension? The decision to treat or not to treat must be made, but what person can comfortably make that decision for another? It is difficult for anyone to measure the steady, small day-after-day costs of treatment against the unlikely but potentially catastrophic cost of nontreatment.

The pure utilitarian assigns responsibility equally for what one does and for what happens, but in daily life one is often regarded as worse than the other. Dunn and Pauker[15] describe a patient with a cyst in a solitary kidney; noninvasive testing failed to dispel the concern that carcinoma may be present in the cyst. In deciding whether to biopsy the kidney, and thus incur a small risk of loss of that kidney with subsequent renal failure, the authors make the explicit assumption that renal failure resulting from the loss of a normal kidney is not worse than that following nephrectomy for cancer. This is a good utilitarian view, but an unlikely estimate of the patient's value system. It is difficult to know with certainty which loss would be worse for the patient; however, one could argue that the accidental loss of a noncancerous kidney might be harder for the patient to accept than a loss necessitated by malignancy. Either action will result in permanent dialysis, but the patient may be grateful to the physician in one instance and resentful in the other. Indeed, Zarin and Pauker observed that patients may be reluctant to participate in mutual decision-making with physicians for several reasons.[16] One reason is because of the anxiety produced by the process of decision analysis itself, with its insistence on specific acknowledgment of ignorance and uncertainty. Another is the patient's anticipation of the regret that he or she will experience for participating in a decision that results in a bad outcome. Such a patient cannot blame the physician for the bad result and so must add the burden of personal guilt to the unhappiness already invoked by the outcome.

One possible approach toward greater physician-patient agreement with regard to risk assessment and management might be to distinguish the distinct components of that task. Pochin[17] described these as the identification of the nature of the harm concerned, the probability that the harm will occur, and the degree or quantity of damage produced if it does occur. The analogy to decision analysis is close. The physician can best identify each risk and fix its probability, but only the patient can say how grave the worst possible scenario would be if it came to pass.

Conclusion

Is there little merit in quantitative approaches to decision making? Not at all. Physicians and their patients, after all, must make decisions; they must somehow choose among therapeutic options, including the decision not to act. No technique yet developed has proven superior to quantitative decision analysis as a means of making one's choices explicit and of enumerating the expected value of each choice. Surprisingly many decisions may show little if any difference in expected utility between choices. In such "toss-up" situations, there is full opportunity to turn at that point to subjective and nonquantitatively based reasons, free of the guilt that one is doing "wrong" by so choosing.[18] In other instances, the choice recommended by the analysis, though mathematically clear cut, may be emotionally or psychologically unacceptable to the patient or the physician. In such cases, considerations of risk seeking or avoidance, financial cost, fear of a given form of treatment, or other personal concerns may override. However, the prior quantitation of probabilities and treatment outcomes has, at the least, created an anchoring structure to stand as a starting point to discussion and decision. Until such time, if it ever comes, when uncertainty has been eliminated from the practice of medicine, quantitative techniques such as decision analysis will serve to establish the foundations upon which further considerations of duty, fairness, and personal preference shape the decisions unique to each patient's needs.

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Acute bone and joint manifestations of sickle cell disease in children

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Bone and joint pain caused by vaso-occlusive crisis is common in patients with sickle cell disease. Dactylitis or the hand-foot syndrome, acute long bone infarction, and sickle cell arthritis or arthropathy may occur in children. Infections, particularly salmonella osteomyelitis and septic arthritis, also occur and may be difficult to distinguish from vaso-occlusive phenomena. In this report the clinical manifestations and the role of scintigraphic studies in distinguishing bone infarction from osteomyelitis and in distinguishing aseptic sickle cell arthritis from septic arthritis will be discussed. The bone and joint complications occurring in 40 out of a total of nearly 600 children with sickle cell disease at our institution during a ten-year period have been reviewed and the results compared with previous written experience.

The term sickle cell disease encompasses homozygous sickle cell anemia (Hgb SS) and other hemoglobinopathies in which the presence of hemoglobin S results in hemolytic anemia. These related hemoglobinopathies include hemoglobin S beta-thalassemia, hemoglobin SC, hemoglobin SE, and hemoglobin SO arab. Sickle cell disease is characterized by chronic hemolytic anemia and is associated with infarction of tissues due to microvascular occlusion by sickled erythrocytes. Almost any organ may be affected by the vaso-occlusive process of sickle cell disease.

PATHOPHYSIOLOGY OF SICKLING

The pathophysiologic consequences of sickle cell disease are a result of genetic mutation within the beta-globin region of the 11th chromosome. This results in the substitution of valine for glutamic acid in the sixth position of the beta-globin chain and produces significant changes in the molecular stability and solubility of the hemoglobin molecule. This is particularly true when deoxygenation occurs. Factors that promote deoxygenation of erythrocytes also enhance sickling and include infection, fever, hypothermia, acidosis, dehydration, and high altitude. Polymerization of deoxyhemoglobin S molecules results in increased viscosity and decreased solubility. Aggregation of these polymers results in deformation of the cell membrane to produce the characteristic sickle-shaped cell. Initially, the sickle deformity is reversible on reoxygenation; however, repeated sickling results both in permanent damage to the erythrocyte membrane and in the formation of irreversibly sickled cells.

While the presence of increased numbers of irreversibly sickled cells correlates with a more severe hemolytic anemia, it appears that tissue injury is instead related to trapping of what had been reversibly sickled cells within the capillary bed under adverse conditions. This trapping results in further stasis, deoxygenation, additional sickling, and ultimately in the occurrence of tissue infarction. An important factor influencing the extent of damage due to vascular compromise is the availability of collateral circulation. The bone marrow is most likely a common site of ischemia and infarction because of high oxygen utilization.

Blood supply to the long bones occurs via a nutrient artery, periosteal vessels, epiphyseal arteries, and perforating metaphyseal vessels (Fig 1).[1] The central nutrient artery and its branches supply blood to the medullary bone, the bone marrow, and a portion of diaphyseal cortex. The proximal and distal branches of the nutrient artery extend to the growth plates at the metaphyseal ends and supply the central area with blood. Periosteal vessels perforate the cortex throughout its length and circumference; branches at the metaphyseal ends are called perforating metaphyseal arteries. The cartilagenous growth plate is supplied by vessels of the epiphyseal ossification center after they pass through the epiphysis. An anastomosis of circumferential epiphyseal and metaphyseal vessels

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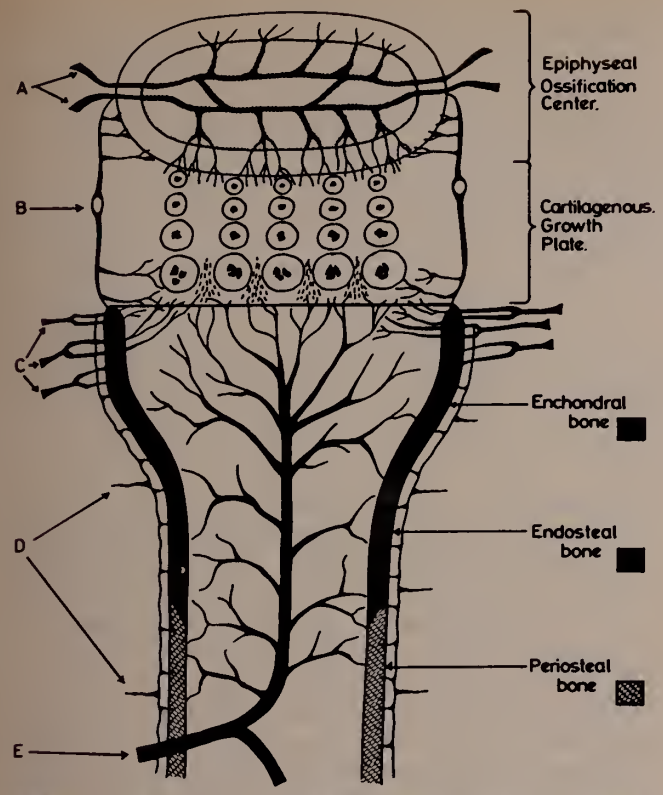

FIGURE 1. Diagram of the blood supply to the long bones. The dividing cells of the cartilagenous growth plate are supplied by epiphyseal ossification center vessels (A) after they pass through the epiphysis. The degenerating cartilage cells at the distal end of the cartilage columns are supplied by the nutrient artery centrally (E) and the perforating metaphyseal vessels marginally (C). The perichondral ring of vessels (B) provide blood supply to both sides of the growth plate. The diaphyseal cortex has a dual blood supply; multiple periosteal vessels (D) support the outer segment and branches of the nutrient artery (E) supply the inner portion of the cortex. A: epiphyseal ossification center vessels; B: perichondral ring vessels; C: perforating metaphyseal vessels; D: periosteal vessels; E: central nutrient artery. (Adapted from Brooks,[1] with permission.)

around the growth plate connects these two circulations even after the cartilagenous growth plate forms what otherwise would be a vascular barrier.

Dactylitis or Hand-Foot Syndrome

Dactylitis, also called the hand-foot syndrome, is commonly the first clinical manifestation of sickle cell disease in children and is due to infarction of the metacarpal, metatarsal, and phalangeal bones.[2,3] The majority of these episodes are seen in children less than 24 months of age, although children up to the age of 5 years may be affected. Generally infants with low fetal hemoglobin levels and high reticulocyte counts are more frequently affected.[3] Since the bone marrow is known to recede from the marrow spaces in the small bones of the hands and feet in older children, dactylitis in this age group is very rare.

Patients with dactylitis are often extremely irritable with puffy, shiny, tender hands and feet (Fig 2) and often with low grade fever. The degree of involvement of the hands and feet may or may not be symmetrical. Early in the course of an acute episode, only soft tissue swelling with no bone change is seen on radiographic examination. In one to two weeks varying degrees of bone destruction and new bone formation are present. Few scintigraphic studies have been done in infants with dactylitis. In our experience, one infant had a bone marrow scan that revealed decreased uptake over the affected bones. Bone scan was done in two children; uptake was decreased in one and increased in the other. Osteomyelitis of the small bones of the hands and feet is seen infrequently in the United States. Management of patients with dactylitis consists of hydration and analgesic therapy; recurrences are common. Recovery is complete with the rare exception that shortening of the involved digit or digits may occur.

Acute Long Bone Infarction

Clinical features. Infarcts of the long bones are common in children and adolescents with sickle cell disease. Bohrer[4] and Keeley and Buchanan[5] reported that nearly 50% of these episodes occurred in children less than 5 years of age. However, in our institution, 65% of these episodes were seen in children above the age of 5 years. Long bone infarctions are predominantly seen in patients with homozygous sickle cell anemia. Patients with sickle-hemoglobin C disease and sickle beta-thalassemia are less frequently affected and tend to be older at the time of long bone infarction.

Affected patients experience acute and deep throbbing pain, which may be incapacitating. Local swelling, tenderness, warmth, erythema, and even induration are commonly seen and adjacent joints may be involved. Patients present with little or no fever, although temperatures of greater than 39°C have been seen in some of our patients. Leukocyte counts may be elevated, usually without a predominance of bands. The erythrocyte sedimentation rate is often elevated. In Nigeria, approximately 95% of long bone infarcts affect the diaphysis, usually the intermediate segment between the metaphysis and the mid diaphysis.[4] The most commonly affected bones are the humerus, tibia, and femur. Long bone infarcts are frequently symmetrical in Nigerian children. However, in a review of 41 episodes of long bone infarction in Dallas, no cases of symmetrical involvement were reported.[5] We have seen symmetrical infarction in five of 40 episodes, usually involving the humeri or tibiae. Pathologic fracture or osteomyelitis complicating acute bone infarction is reported to be a frequent occurrence in Nigeria, but these complications are uncommon in the United States.

FIGURE 2. Infant with dactylitis.

TABLE I. Bone Infarction in Sickle Cell Disease: Scintigraphic Findings

Author	Bone scan			Marrow scan			Gallium scan	
	↑	↓	N	↑	↓	N	↑	N-↓
Hammel et al*	3/3	—	—	—	3/3	—	—	—
Kim et al (8)	12/22	10/22	—	—	22/22	—	—	—
Majd (19)	3/3†	—	—	—	—	—	—	3/3
Keeley et al (5)	6/10	3/10	1/10	1/3	1/3	1/3	4/4	—
Milner (12)	—	—	—	—	13/13	—	—	—
Amundsen et al (13)	19/20	1/20	—	—	—	—	12/20	8/20
Armas et al (14)	8/14‡							14/14
Koren et al (9)	13/38	18/38	7/38	—	—	—	—	—
Rao et al (10)	14/22	3/22	5/22	—	17/18	1/18	—	—

* Hammel CF, Denardo SJ, Denardo GL, Lewis JP: Bone marrow and bone mineral scintigraphic studies in sickle cell disease. *Br J Haematol* 1973; 25:593.
† Others had decreased or increased uptake.
‡ In six others, the uptake was either decreased, increased, or normal.
↑: increased; ↓: decreased; N: normal.

Radiologic findings. Initially no changes are evident, but new bone formation superimposed on dead trabeculae results in increased roentgenographic density in seven to 14 days. A less common but more distinctive finding, "cortex within a cortex," consists of a layer of dense bone near the periphery of the medullary canal but separated from the inner aspect of the cortex by a narrow lucent zone.[6] Radiographic distinction from osteomyelitis is not possible.

We have found that a bone marrow scan is particularly useful in evaluating sickle cell patients with bone pain. While useful in some cases, a bone scan does not generally permit distinction between bone infarction and osteomyelitis.

Technetium-99m methylene diphosphonate (MDP) is the optimal agent for bone scanning. Radioisotope uptake by bone reflects mineral turnover and osteoblastic activity. The usual dose of MDP is 200 μCi/kg of body weight. An immediate blood pool image is obtained within five minutes of injection, followed by delayed scanning in 90 to 120 minutes. Uptake of isotope depends on vascular supply and the presence of new bone formation[7] (Table I). In the first few days after bone infarction, there may be an area of decreased uptake on bone scan (Fig 3).[8-10] This is followed by an area of increased uptake five to ten days later indicating reactive new bone formation (Fig 4). This increased uptake may persist for months. When evaluating a long bone lesion, the opposite extremity should also be scanned for comparison since long bones in sickle cell disease show a diffusely increased uptake, especially in the lower extremities.

Technetium-99m sulfur colloid is widely used for bone

FIGURE 3. Infarction of upper right tibia in a 13-year-old girl. The anterior TC-99m MDP bone scan shows area of decreased uptake in the upper right tibia with increased uptake just below the infarct.

FIGURE 4. Infarction of right femur in a 5-year-old girl. The anterior TC-99m MDP bone scan shows area of decreased uptake in the proximal right femur with increased uptake in the distal part just above the knee.

marrow imaging and has a half-life of six hours. The usual dose for children is 150 μCi/kg body weight and the imaging is done in 15 to 30 minutes. In normal adults, activity of the isotope is distributed in reticuloendothelial cells of the bone marrow (10%), liver (80%), and spleen (10%). In sickle cell disease, the bone marrow is hypercellular and on scanning provides a symmetrical and relatively homogenous appearance, even in adults.[7] Bone marrow scanning is ideal for evaluating long bones. However, because of interference by the hepatic image, bone marrow scan is not suitable for evaluation for lower thoracic and upper lumbar vertebrae or lower ribs.

Bone marrow scanning abnormalities may be the only evidence of ischemia from a vaso-occlusive process involving the skeleton. Soon after the onset of bone pain, the bone marrow scan will reveal an area of decreased uptake at the site of marrow infarction[7-8,10-11] (Fig 5). The area of decreased uptake is often greater than that suspected clinically, and may be seen for weeks to months after an episode of infarction.[10] It has been shown that younger patients are more likely than adults to repopulate their marrow after vaso-occlusive ischemia.[12]

Uptake of 67-gallium has been variable in the few sickle cell patients with bone infarction studied[13,14] (Table I). While one research group had advocated its use in conjunction with the bone scan to distinguish bone infarction from osteomyelitis,[13] the relatively large radiation dose needed and the variable findings make 67-gallium scanning less useful.

Bone marrow scanning using technetium-99m sulfur colloid appears to be the most informative of the three scintigraphic studies available. Decreased uptake on marrow scan is sensitive and, as discussed below, appears to be specific for bone infarction.

FIGURE 5. Infarction of right femur in a 10-year-old girl. The anterior TC-99m sulfur colloid marrow scan shows markedly decreased uptake in the entire right femur.

Osteomyelitis

Persons with sickle cell disease have an increased susceptibility to salmonella osteomyelitis as compared with normal individuals.[15,16] While reasons for this are not clear, Adeyokunnu and Hendrickse[16] have suggested the following mechanism of pathogenesis. In areas where gastrointestinal infection with salmonella is common, hematogenous spread is possible by sickle-related infarction of the intestine. Organisms may then settle in necrotic tissues such as bone and bone marrow infarcts that are favorable sites for infection. However, in our experience children with osteomyelitis did not have scintigraphic evidence of recent marrow infarction.

Further evolution of infection may result from immunologic abnormalities observed in sickle cell patients. Diminished serum bactericidal activity against salmonella, which correlates well with a defective alternate complement pathway, was demonstrated in nearly 40% of patients with sickle cell anemia.[17] In addition, elevated transferrin saturation may increase susceptibility to salmonella infection. However, there was a poor correlation between transferrin saturation and defective serum bactericidal activity against salmonella[17]; infants and young children with normal transferrin saturation are nonetheless prone to salmonella infection. Hyposplenia and impaired opsonization of polysaccharide antigens are well described in reference to *Streptococcus pneumoniae* infection; these or similar defects may also contribute to the evolution of osteomyelitis.

Clinical features. The diagnosis of osteomyelitis is suspected in any patient with sickle cell disease who has bone pain and fever. This is particularly true in the very young child. Among 57 children with salmonella osteomyelitis and sickle cell anemia reported by Adeyokunnu and Hendrickse,[16] 40% were below the age of 2 years and an additional 40% were aged 2 to 5 years. Seven out of eight children with sickle cell disease and osteomyelitis seen in our institution over the last ten years were under 5 years of age. In most series, boys predominate.

The site of osteomyelitis in Nigerian children varies with age.[16] The most common sites of involvement are the bones of the hands and feet in infants and the long bones of the extremities in older children. In most patients, the lesions are bilateral and symmetrical. While osteomyelitis of the bones of the hands and feet is quite uncommon in the United States and Great Britain, long bones of the upper extremity are commonly affected. However, symmetrical involvement is unusual. Patients generally present with fever, pain, and swelling of an extremity. The temperature in most patients with osteomyelitis is above 39°C. Young infants often present with high fever and signs of sepsis. In some patients, the diagnosis of osteomyelitis is suspected only when signs and symptoms thought

to be due to vaso-occlusive crisis persist beyond seven to ten days. Bone scan or radiographs done because of poor response to antibiotics in patients with bacteremia may reveal evidence of bone involvement. Generally, the leukocyte count is high and there is a predominance of neutrophils and band forms; the sedimentation rate is usually elevated. Hypoplastic crisis is also frequently noted in patients with osteomyelitis.

Isolation of bacteria from bone aspirate or from blood in a patient with signs of bone involvement will confirm the diagnosis of osteomyelitis. In a review by Givner and colleagues[18] of osteomyelitis in 84 patients with sickle cell disease, salmonella accounted for 74% of the bacteria isolated. Staphylococci (10%) and *S. pneumoniae* (5%) were

FIGURE 6A. Osteomyelitis of the left humerus in a 6-year-old girl. Radiograph of the left humerus shows areas of bone destruction and periosteal reaction.

TABLE II. Osteomyelitis in Sickle Cell Disease: Scintigraphic Findings

Author	Bone scan			Gallium scan		Marrow scan	
	↑	↓	N	↑	↓	↑	N
Majd (19)	1/1	—	—	—	—	—	—
Wethers et al (20)	2/3	—	1/3	1/1	—	—	—
Amundsen et al (13)	2/4	1/4	1/4	4/4	—	—	—
Koren et al (9)	2/2*	—	—	2/2*	—	—	—
Rao et al (10)	7/8	—	1/8	1/1	—	—	5/5

* No bacteriologic confirmation of osteomyelitis.
↑: increased; ↓: decreased; N: normal.

the other common pathogens. Of the eight cases of osteomyelitis in children treated in our institution in the past ten years, five cases were due to salmonella and three were due to *S. pneumoniae*. The ages of patients with salmonella osteomyelitis ranged from 19 months to 9 years, and only one patient was younger than 2 years. In contrast, all three patients with *S. pneumoniae* osteomyelitis were younger than 19 months of age; they had yet to receive pneumococcal vaccine and two out of three were noncompliant to the prescribed penicillin prophylaxis.

Radiologic findings. These are similar to the findings in patients with bone infarction and thus do not help distinguish infarction from osteomyelitis (Fig 6A).

There are few reports available of scintigraphic findings in sickle cell patients with osteomyelitis.[10,13,19,20] As indicated in Table II, most infected bones (14/18) showed increased uptake on bone scan (Fig 6B). However, decreased[13] or normal uptake[13,20] may also be seen. All eight patients showed increased uptake on gallium scan. However, it must be remembered that both studies (bone scan and gallium scan) may also demonstrate increased uptake in bone infarction (Table I). While uptake by bone marrow scan is diminished in 95% of patients with bone infarction, five patients with osteomyelitis showed normal uptake at the infected site (Fig 6C). Bone scan revealed increased uptake in four of these patients; the bone scan was normal in one. However, the latter patient did have increased uptake on the blood flow phase of the scan. Bone scan may be useful in looking for osteomyelitis in patients who do not manifest local findings (eg, an infant with bacteremia or an older child with persistent fever responding poorly to antibiotic therapy). An area of increased uptake, particularly in a patient with bacteremia, is highly suggestive of osteomyelitis. In such cases, aspiration of the suspected site is indicated for diagnostic purposes. The major role of a bone marrow scan in patients with sickle cell disease is in distinguishing bone infarction from osteomyelitis. A normal marrow scan in a patient who has localized bone pain, signs of local inflammation, and fever suggests the diagnosis of osteomyelitis. Confirmation of the diagnosis remains contingent upon the isolation of the microorganism from the bone aspirate, blood, or both.

Sickle Cell Arthritis

Joint symptoms are common in patients with sickle cell disease and are usually related to infarction of bone marrow and bone adjacent to the affected joint. Diggs[21] described the synovial fluid in knee joints as being purulent exudates that were negative for bacteria on direct exami-

FIGURE 6B. The anterior TC-99m MDP bone scan shows markedly increased uptake in the upper left humerus.

nation and culture. Schumacher and coworkers[22] reported synovial fluid as being noninflammatory even though patients manifested swelling of the joint associated with warmth and limitation of movement. Synovial biopsy specimens revealed microvascular thrombosis, lining cell proliferation, and rare inflammatory cells. Many of these patients had evidence of infarction of the adjacent bone.

Bone marrow scan was utilized by Alavi and associates[23] to distinguish arthritis due to a vaso-occlusive process from arthritis due to other causes. Bone marrow scans in eight out of 12 patients confirmed the presence of marrow infarction in an adjacent bone; the remaining four patients with normal marrow scans had findings such as fracture or osteoarthritis to explain the joint symptoms. Hanissian and Silverman[24] described recurrent acute arthritis in four children with sickle cell disease in whom the synovial fluid showed a moderate inflammatory response. Three of these four children had evidence of bone infarction which was thought to be old.

In the past ten years, 11 children in our sickle cell patient population presented with 12 episodes of sickle-related arthritis. This group represents only those patients who had arthrocentesis, bone marrow scan, or both as part of their evaluation. The elbow and knee were the most frequently involved joints; in two of the 12 episodes the elbows were involved bilaterally. Most patients manifested swelling, warmth, and tenderness of the joint with limitation of motion. The synovial fluid was either serous or serosanguineous in six out of seven episodes; one patient had purulent fluid that was sterile. Bone marrow scan revealed evidence of infarction in the adjacent bone in eight of nine episodes. All patients with sickle-related arthritis recovered completely with hydration and analgesic therapy. This aseptic arthritis is the most common form of acute arthritis in children with sickle cell disease and is due to infarction of the bone marrow and bone adjacent to the joint. When septic arthritis is a serious consideration, bone marrow scan and aspiration of synovial fluid are helpful in the differential diagnosis.

Septic Arthritis

Septic arthritis is uncommon in patients with sickle cell disease. Although salmonella is rarely reported to cause arthritis, in one report it was isolated from the synovial fluid in four of nine infected joints; *Pseudomonas aeruginosa*, *Escherichia coli*, and *Proteus mirabilis* were the other isolates found.[25] Three cases of septic arthritis in children with sickle cell disease occurred at the Health Science Center at Brooklyn over a ten year period. All three patients were younger than 2 years of age, and in two out of three the hip or shoulder joint was involved; these are rare sites for sickle-related arthritis. *S. pneumoniae* was the etiologic agent in two patients and salmonella was the cause in one. Consistent with the observations of Ebong,[25] all three children with septic arthritis in our institution had osteomyelitis of the adjacent bone as demonstrated by compatible findings on bone radiographs and bone scan. The bone marrow scan that was done in two patients revealed normal uptake. Thus, bone marrow scan may again be useful in distinguishing infarction from infectious processes. Definitive diagnosis of septic arthritis is established by isolation of a pathogen from the synovial fluid.

Patient Management

Since infarction is much more common than infection in patients with sickle cell disease, conservative management will suffice in the majority of children. Treatment should include fluids given at a rate of at least twice the usual basal requirement, together with careful monitoring of intake and output, body weight, and electrolytes. Sufficient analgesia should be provided for pain relief; this usually requires a narcotic agent given parenterally and around the clock for the first 24 to 48 hours of hospitalization. In patients who ultimately prove to have long bone infarction or sickle-related arthritis, inflammatory symptoms and signs generally resolve over a period of three to seven days without sequelae. In the unusual patient who shows no improvement after four to six days, packed red

FIGURE 6C. The posterior TC-99m sulfur colloid marrow scan shows normal uptake by both humeri.

cell transfusion or partial exchange transfusion may be beneficial.

In patients with persistent high fever or prominent local findings, infectious causes of bone or joint swelling must be strongly considered. Bone marrow scanning may be useful in such patients or in patients in whom antibiotics have been empirically started prior to full evolution of a localized inflammatory process. On occasion osteomyelitis may be "partially treated" and the culture may be spuriously sterile. Diminished uptake of isotope in the affected area supports the diagnosis of vaso-occlusive crisis and conservative management may be continued. Normal uptake, however, should provoke a more aggressive attempt to isolate bacterial pathogens, including multiple blood cultures and aspiration of the inflamed area. Joint aspiration may be accompanied by an attempt to aspirate pus subperiosteally from an adjacent bone.

Antibiotic therapy may then be instituted to provide coverage for the most common pathogens, such as salmonella, *S. pneumoniae*, and *Staphylococcus aureus*, unless more specific therapy is given based on a Gram stain of aspirated fluid. Salmonella osteomyelitis, if confirmed, requires appropriate intravenous antibiotic therapy for four to six weeks, and an additional four to six weeks of oral antibiotic therapy. Serum bactericidal assays should be monitored serially. Four weeks of intravenous antibiotic therapy, followed by an additional two to four weeks of oral antibiotic therapy, should be adequate to treat osteomyelitis due to *S. pneumoniae* or *S. aureus*. Surgical drainage and debridement may be required in some children. In the rare occasion that septic arthritis occurs without osteomyelitis, two to three weeks of intravenous antibiotic therapy, perhaps followed by an additional two to three weeks of oral antibiotic therapy should suffice. Joint aspirations as often as twice a day may be required early in the treatment course to minimize the risk of permanent damage to the joint. Generally the prognosis for full recovery is good.

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SICKLE CELL ANEMIA

The x-ray changes in the long bones and skull in sickle cell anemia have been frequently described and are well known. The first really comprehensive study of the bone changes in sickle cell anemia was made in 1937 by Diggs, Pulliam, and King who correlated the gross and microscopic findings with the x-ray appearance. They stated that "the bones of the wrist, hands, ankles, and feet present no striking roentgenographic changes." Osteoporosis of moderate degree was noted occasionally in the cancellous bones of the hands and feet.

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(*NY State J Med* 1957; 57:1403-1408)

Post urethroplasty squamous cell carcinoma

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Urethral stricture has long been associated with the occurrence of squamous cell carcinoma.[1] Patients with long-standing stricture disease are at the highest risk of developing a malignancy. However, once a successful urethroplasty has been performed the occurrence of urethral carcinoma at the reconstructed site is rare. The following report is of a patient who developed a squamous cell carcinoma at the site of urethroplasty 11 years after stricture repair. These findings are compared with the other six patients reported in the literature[2-6] regarding tumor presentation and location, clinical course, and treatment.

CASE REPORT

A 72-year-old man presented in November 1983 to the urologic service with acute urinary retention requiring suprapubic drainage. He initially was seen in 1962 with a distal urethral stricture secondary to gonorrhea requiring urethral dilatations every two to three months over a ten-year span that culminated in 1972 with a one stage Horton-Devine patch urethroplasty utilizing scrotal skin. Physical examination on admission to the hospital was remarkable for an indurated scrotum and a hard irregular prostate. No inguinal nodes were palpable.

Laboratory findings revealed elevated serum BUN and creatinine levels, a normal serum acid phosphatase level, a serum calcium level of 13.2 mg/dL (normal, 8.7 to 10.7 mg/dL), and a normal serum parathyroid hormone (PTH) level. Urine culture was negative and a chest radiograph was unremarkable. A retrograde urethrogram demonstrated an irregular penile urethra with multiple filling defects (Fig 1). Excretory urogram showed normal upper tracts with a severely trabeculated bladder with multiple diverticulae. Cystourethroscopy revealed a frond-like growth along the lateral aspects of the patch graft in the bulbar urethra of which cold cup biopsy specimens were taken. The bladder and proximal urethra appeared free of tumor and transperineal needle biopsies of the prostate were also performed. The urethral biopsy revealed squamous cell carcinoma while the prostate biopsy showed a Gleason's 4 adenocarcinoma. Metastatic work-up was negative.

FIGURE 1. Retrograde urethrogram revealing irregular penile urethra with multiple filling defects.

Prior to the initiation of therapy the patient left the hospital of his own accord and one month later returned with an ulcerating mass at the perineal-scrotal junction with a draining urethrocutaneous fistula (Fig 2) that was lined with a poorly differentiated squamous cell carcinoma. The patient underwent surgical therapy that consisted of en bloc partial penectomy, partial scrotectomy (Fig 3), bilateral orchiectomy, and the formation of a perineal urethrostomy. The surgical margins at the time of surgery were free of tumor.

The patient's postoperative course was uneventful. The wound healed and he remained continent by voiding via the perineal urethrostomy. His serum calcium level remained elevated, never falling below 11.5 mg/dL despite therapeutic intervention. At 17 month follow-up no evidence of recurrence was seen at the surgical site. However, squamous cell carcinoma was found at the suprapubic site. Metastatic work-up at this point still remained negative.

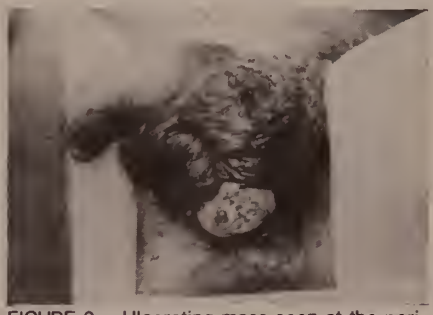

FIGURE 2. Ulcerating mass seen at the perineal scrotal junction with a urethrocutaneous fistula.

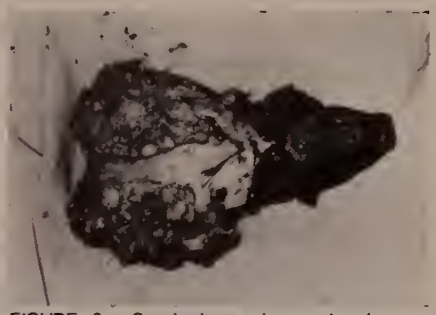

FIGURE 3. Surgical specimen showing en bloc partial penectomy and partial scrotectomy.

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TABLE Ia. Presentation of Carcinoma Developing Post Urethroplasty

Case	Age	Type of urethroplasty	Interval between urethroplasty and diagnosis of cancer	Histology	Location of tumor	Clinical presentation
1	60	One-stage Denis-Browne	5 yr	Squamous	Distal	Periurethral abscess; urethral cutaneous fistula
2	68	Two-stage Johanson	10 mo	Squamous	Distal	Priapism secondary to tumor in corpora; decrease in urinary stream
3	67	Two-stage Turner-Warwick	4 yr	Squamous	Proximal	Slower stream; mass in scrotum; urethral perineal fistula
4	79	Two-stage Turner-Warwick	8 yr	Squamous	Distal	Ulcerating inguinal nodes
5	74	Two-stage Turner-Warwick	5 yr	Squamous	Distal	Slower stream; palpable inguinal nodes; urethral cutaneous fistula; induration along urethra
6	50	Two-stage Johanson	2 yr	Epidermoid	Proximal	Perineal pain; decreased stream; urethrocutaneous fistula; perineal and inguinal masses
7	72	One-stage Denis-Browne	11 yr	Squamous	Distal	Urinary retention; perineal mass; urethral perineal fistula

Discussion

There is a well known association between urethral carcinoma and stricture disease. There is also little doubt that stricture with its associated dilatations, infection, and epithelial injury may, in some cases, stimulate the formation of carcinoma.[2] Although squamous metaplasia is a common occurrence at stricture sites, it is often questioned whether this lesion is premalignant.

In a study of 70 patients post mortem with strictures, Owor[7] found squamous metaplasia in 86% of the patients. He postulated that the development of squamous metaplasia is due to chronic irritation and that the metaplasia may then undergo malignant changes.[7] However, in a study by Colapinto, patients with strictures who appeared to have squamous metaplasia did not subsequently develop carcinoma.[4] It appears then that squamous metaplasia cannot be solely implicated as a premalignant lesion.

We reviewed seven cases of urethral carcinoma that developed post urethroplasty (Table I). In the reported cases, no mention is made of squamous metaplasia as a preexistent lesion. The ages of patients studied ranged from 50 to 79 years. Five patients underwent two-stage repairs and no mention of cancerous lesions was made after the first stage. Five patients presented with distal lesions while two had proximal tumors. The interval from urethroplasty to the development of the carcinoma ranged from ten months to 11 years, with the average being five years (Table II). The presenting signs and symptoms included bleeding, palpable inguinal and scrotal masses, urethrocutaneous fistulas, changes in voiding patterns, and periurethral abscess (Table III). In terms of survival, four patients died due to the tumor within one year, two had only short term follow-up, and one patient had no evidence of disease at four years (Table IV).

TABLE Ib. Treatment and Final Outcome of Urethral Carcinoma Post Urethroplasty

Case	Treatment	Result
1	En bloc total penectomy; scrotectomy; orchiectomy; bilateral inguinal node dissection	No evidence of disease at 4 yr
2	Penectomy to urogenital diaphragm	Dead of tumor at 7 months
3	Total penectomy; urethrectomy; en bloc removal of crura; U-G diaphragm; cystoprostatectomy; bilateral inguinal node dissection	Dead of tumor at 2 mo
4	Total penectomy; scrotectomy	Dead of tumor at 2 mo
5	Radiotherapy to penis and inguinal regions; bleomycin; palliative penile amputation	Dead of tumor at 1 yr
6	Bleomycin; cisplatinum; methotrexate	No progression of tumor at 3 mo
7	Partial penectomy; orchiectomy; scrotectomy	No evidence of disease at 3 mo

TABLE II. Clinical Findings

Age	50-79 yr
Type of urethroplasty	One stage: 2 Two stage: 5
Location	Proximal: 2 Distal: 5
Interval urethroplasty to carcinoma	10 mo to 11 yr

Besides allowing relief of symptoms, urethroplasty removes the chronic irritation and may prevent, in the future, the formation of a carcinoma as is evidenced by the few reported cases. However, if the urethroplasty is not successful, continued irritation occurs and the individual may still develop a carcinoma at a later date. For this reason patients who develop worsening symptoms or signs post urethroplasty, even though they most likely have a recurrent stricture, should be thoroughly investigated with an index of suspicion for urethral carcinoma. Work-up should include retrograde urethrography, cystourethroscopy, biopsy when indicated, bimanual examination, and computed tomographic scan if necessary. Cytologic examination of the urethral secretions or urine, which is easily obtainable, aids in early diagnosis.[8]

TABLE III. Presenting Signs and Symptoms

Urethrocutaneous fistula	5
Increased difficulty in voiding	5
Abscess/mass	4
Palpable inguinal nodes	3
Tumor along shaft	2

TABLE IV. Final Outcome

Location	Treatment	Outcome
Proximal	1: Radical surgery	Dead of tumor at 2 mo
	1: Chemotherapy	Controlled at 3 mo
Distal	4: Radical surgery	No evidence of disease at 4 yr
		Dead of tumor at 7 mo
		Dead of tumor at 2 mo
		No evidence of disease at 4 mo
	1: Radiotherapy + chemotherapy	Dead of tumor at 1 yr

From the cases reported above it appears that patients who undergo urethroplasty should be followed for a long period of time; if symptoms recur carcinoma should be ruled out early. The patients we saw who presented with evidence of tumor such as a perineal mass, abscess, or fistula had a dismal prognosis and a progression of their disease so great as to make only a short term survival.

Radical surgery did not, at the time of diagnosis, affect the prognosis. However, it did control the local symptoms (ie, foul odor, fungating mass, fistula, and improvement of patient discomfort). Chemotherapy and radiotherapy also did not improve prognosis. An interesting point is that the patient reported here had an increased serum calcium with a normal parathyroid hormone level, supporting the diagnosis of pseudohyperparathyroidism secondary to perhaps an unfound focus of metastatic tumor. This is common with other types of malignancy such as lung, gastrointestinal, and renal, and is probably due to a parathyroid-like hormone that is secreted by the tumor.[3]

In conclusion, it appears that early diagnosis is essential for improving survival rates. However, urethroplasty does not prevent the formation of urethral carcinoma; if it does occur, current results with surgery, chemotherapy, or radiotherapy are poor.

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See also pp 232–233.

Aneurysm and seroma formation in a velour Dacron prosthesis

Maurizio Daliana, MD, John A. Pagnozzi, MD, Jere W. Lord, Jr, MD

Several reports of true aneurysms, both fusiform and saccular, developing in knitted velour Dacron prostheses years after implantation have been recently published in the literature.[1–3] Three explanations have been offered for this phenomenon. These include damage to the prosthesis at time of implantation, broken textile fibers with distension of the graft, and expansion of the knit.

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Blumenberg and associates[4] have provided a comprehensive review of the literature concerning the development of perigraft seromas complicating prosthetic arterial grafts. The researchers state that the seromas contained clear serum without infection, and that the grafts were poorly incorporated into the surrounding tissues.

We report here a patient in whom both a fusiform-saccular aneurysm and a large localized seroma appeared 11 years after an axillo-axillary bypass for severe ischemia of the left arm and hand due to atherosclerotic occlusion of the proximal subclavian artery. An 8 mm knitted velour Dacron prosthesis was utilized for the bypass.

Case Report

A 65-year-old woman was admitted to the hospital on October 30, 1973 because of severe pain in the left arm with activity and numbness and tingling of the left hand. She had smoked three packs of cigarettes daily for more than 30 years. There was a 40 mm Hg differential between the right and left arm blood pressures and weak brachial, ra-

dial, and ulnar pulses on the left side. Oscillometric deflections were 4.0/120 on the right forearm and 1.0/100 on the left. An angiogram revealed normal right subclavian and carotid arteries; however, total obstruction of the first portion of the left subclavian artery with reconstitution at the clavicular area from the left vertebral artery was noted. The axillary and brachial arteries appeared unremarkable. There had been no symptoms of subclavian steal.

On November 2, 1973 an 8 mm Dacron prosthesis was joined to a 10 mm right axillary artery just below the clavicle, tunneled deeply subcutaneously and joined to a small (5 mm) weakly pulsatile left axillary artery. The postoperative course was uneventful. The radial pulses were equally strong on palpation, oscillometric deflection was 3/120 at each forearm, and blood pressure readings were found to be 130/60 bilaterally.

A follow-up angiogram on October 17, 1974 showed no stenosis of either anastomosis and no dilatation of the prosthesis. However, despite repeated warnings the patient continued to smoke cigarettes. On July 21, 1975 a chest radiograph, warranted by pulmonary symptoms, revealed a small lesion of the left upper lobe. Abnormally low arterial blood gases improved with intermittent positive pressure breathing (IPPB) four times a day for several days. On July 28, 1975 a left upper lobectomy was performed for a small adenocarcinoma.

Except for exertional dyspnea caused by emphysema the patient was well until October 1984, when a pulsatile mass appeared in the left manubrial region of the prosthesis. The mass progressively increased in size during the ensuing three months. Examination revealed a strongly pulsatile mass 4 × 5 cm in size with no redness or tenderness. A loud systolic bruit was audible over the mass and there was minimal dilatation of the lateral aspects of the prosthesis (Fig 1). It was our clinical impression that the large pulsatile mass was a true aneurysm of the Dacron prosthesis. For this reason consideration of

FIGURE 1. A pulsatile mass in an axillo-axillary bypass.

aspiration—suggested by Blumenberg and his associates for seromas—was discarded as potentially hazardous.

On January 11, 1985 the prosthesis was removed, along with a sac 5 cm in diameter that contained moderately thick, yellowish fluid thought to be purulent. Aerobic and anaerobic cultures of the fluid failed to grow any organisms. Continuity of each axillary artery was maintained. Recovery was uneventful and the left upper extremity has since remained asymptomatic.

Pathologic examination revealed that the prosthesis was dilated throughout to 15 mm except at the midpoint, where it measured 25 mm in diameter (Fig 2). The sac, which contained 100 mL of cloudy fluid, showed a foreign body giant cell reaction with cholesterol crystals in the surrounding tissue on microscopic examination.

FIGURE 2. Specimen showing aneurysmal dilatation of prosthesis and seromal sac.

Discussion

Two relatively uncommon complications of knitted Dacron prostheses appeared in the patient described 11 years following implantation. The entire prosthesis was fusiformly aneurysmal with a saccular component at its midpoint. This area was surrounded by a spherical collection of fluid that was thicker and darker than the typical seroma. Sterility of the fluid ruled out infection and histologic examination was compatible with the diagnosis of a seroma.

Aneurysmal dilatation of knitted Dacron prostheses has been studied carefully in vitro by several authors[1,2] who concluded that yarn slippage occurs early after implantation and that a second stage of failure is related to the characteristic behavior of individual fibers subjected to load. Stretching and releasing of the material with each pulsatile wave may ultimately lead to structural fatigue and fiber breakage.

It is possible that the marked dilatation of the prosthesis at its central portion allowed serum to transudate, setting up a foreign body-like reaction with giant cells and cholesterol crystals.

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Pleomorphic adenoma of the breast with positive estrogen receptors

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The benign mixed tumor of the salivary gland type is a rare tumor of the breast,[1] described first in the French literature by Lucène in 1906 and cited more recently by Nabert and associates.[2] It is characterized by glands and tubule-forming epithelial cells lying in a myxomatous-chondroid matrix,[3] thus sharing histologic similarity to the mixed tumor of salivary gland origin.[4] These lesions are usually resected for a clinical suspicion of cancer. The current definition of the mixed tumor emphasizes a prominent role of the myoepithelial cell in the formation of this lesion.[5]

Quantification of the functional activity of the epithelial cell is of critical importance and forms the basis for hormonal manipulation in carcinoma of the breast.[6,7] However, such activity is not unique to cancer of the breast and has been found in benign lesions as well.[8,9] We recently studied a patient with a mixed tumor in whom the clinical diagnosis of cancer was made, a tylectomy performed, and the estrogen receptor content found to be positive by our criteria of greater than 10 fmol/mg cytosol protein as being positive.

CASE REPORT

A 75-year-old woman was referred to another hospital for the evaluation of a small, well-circumscribed mass in the left breast located at 6 o'clock 2 cm below the nipple. The diagnosis of cancer was based on the suspicious nature of a neoplasm found in an elderly woman. The patient sought a second opinion at Montefiore Medical Center. A mammogram performed at that time was considered to be consistent with a benign lesion. The patient had a history of fibrocystic disease of the breast repeatedly aspirated and ultimately resected in 1940 with apparent therapeutic success. The patient also had a hysterectomy for presumed fibroids in 1940. Her medical history was otherwise unremarkable. Aspiration cytology of the breast lesion showed a single cluster of benign duct cells. A tylectomy was performed one month later with a clinical diagnosis of early breast cancer. The tissue was sent to both the surgical pathology and the estrogen-binding laboratories. The estrogen receptor level was 12 fmol/mg of cytosol protein, and the progesterone receptor level was 3 fmol/mg cytosol protein.

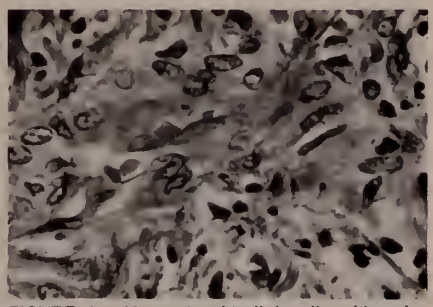

FIGURE 1. Nest of epithelial cells with spindled myoepithelial cells. (Hematoxylin and eosin stain; original magnification × 400.)

On pathologic examination the specimen consisted of a piece of yellow-tan fibroadipose tissue with a centrally located white nodule measuring 1 cm in diameter. Microscopically the nodule had the typical appearance of a benign mixed tumor of salivary gland type with epithelial and myoepithelial components (Fig 1) in a loose myxoid stroma (Fig 2). The surrounding breast tissue was atrophic. The PAS and PAS/d stains confirmed the presence of glycogen in the epithelial cells and focally in the stroma of the tumor. Mucicarmine stain was negative. Immunoperoxidase stains for S-100 protein were positive (Fig 3). Although the follow-up period was extremely short (16 months), the patient reported no change in status, nor had there been a recurrence of the lesion.

DISCUSSION

Mixed tumor or pleomorphic adenoma of salivary gland type occurring in the breast was first described in 1906 by Lucène.[10] In the English literature, it was considered synonymous with the fibroadenoma[11] and since the two lesions were not separated until 1969,[12] the true incidence of this unusual lesion is not known. The myoepithelial cell is

FIGURE 2. Loose chondromyxoid stroma in the salivary gland type mixed tumor, with sharp demarcation from the surrounding breast tissue. (Hematoxylin and eosin stain; original magnification × 40.)

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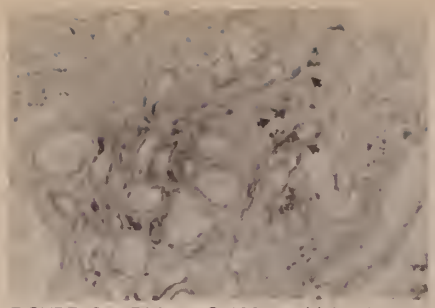

FIGURE 3. Diffuse S-100 positivity (arrowheads) of the myoepithelial cells in the mixed tumor. (Immunoperoxidase, S-100; original magnification × 100.)

widely accepted as the cell of origin of the mixed tumor,[13,14] regardless of location; this has been confirmed both immunohistochemically[15] and ultrastructurally.[16,17] The myoepithelial cell has been found to "mark" with S-100, an acidic polypeptide composed of an alpha and beta chain originally isolated in the bovine brain.[18] Although it was initially thought to be specific for nervous tissue, S-100 positive staining by the immunoperoxidase technique may be seen in the neural crest, ductular epithelial cell of the salivary glands, and breast, as well as myoepithelial cells.[19]

The case presented here is typical of those reported in the literature.[2,3,10,12,18-22,27] All of the patients studied were female with one notable male exception,[20] and ranged in age from 23 to 78 years. The women presented with painless lumps measuring from 0.8 to 4.5 cm in diameter that were well circumscribed and firm to gritty to cutting. There was a statistical "outlier" who had a much larger lesion measuring 20 cm in diameter and weighing 2300 g that presented with bloody discharge.[21]

Parenthetically, in the 13 cases in which laterality was noted, 12 were reported on the right side. These tumors showed small cords and islands of glands having a two-cell layer (cuboidal epithelium surrounded by myoepithelium) and were bathed in a chondromyxoid stroma high in glycogen content. The bone formation frequently seen in both benign[3] and malignant[23,24] mixed tumors of the breast was not present in our case.

It should be remembered that while the benign mixed tumor is a rare lesion in man, it is quite common in dogs. Moulton and colleagues[25] found that 10 to 45% of all tumors in dogs arise in the breast, of which approximately 40% are benign mixed tumors. Interestingly, when the dogs were separated into neutered and nonneutered groups, the latter group had a higher proportion of mixed tumors, suggesting a more than casual hormonal influence in the formation of these neoplasms. When neoplasms were experimentally induced in dogs by the use of oral contraceptives, benign mixed tumors comprised from zero to 10% (depending on the agent used) of the newly-formed nodules,[26] further substantiating the evidence that the benign mixed tumor may be a hormonally reactive neoplasm.

More unusual is the relatively high level of estrogen activity in a lesion that shows relatively small amounts of epithelium. Lee[28] noted that the proportion of epithelial to stromal component would influence the amount of extracted receptor protein, indicating that estrogen binding activity is at least in part a function of the quantity of epithelium in the breast tissue. Positive estrogen-[8,9] as well as progesterone-[29,30] binding activity commonly occurs in benign neoplasms of the breast. Allegra and colleagues[8] studied 55 benign lesions of the breast and found that 38% of the entire group was positive with greater than 10 fmol/mg cytosol protein. Of the benign lesions reported by Martin and associates,[9] 42% were positive, although their criteria for positive was slightly lower (7 fmol/mg cytosol protein); they concluded that the estrogen receptor levels of benign breast lesions were higher in younger women with short clinical histories and dense cellularity in the lesions. When that activity was examined according to histological type, 25% of the fibrocystic lesions and 55% of the fibroadenomas were positive; the remaining benign lesions were negative. Our search of the literature leads us to believe that this is the first reported case of positive estrogen binding activity in a mixed tumor of the human breast. As the mixed tumor is thought to derive from the myoepithelial cell, further studies are warranted to delineate this cell's contribution to the level of receptor activity measured in both benign and malignant lesions of the breast.

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See also pp 000-000.

Simultaneous occurrence of fibromatosis and infiltrating lipoma in the gastrocnemius muscle

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Extra-abdominal fibromatosis (desmoid) and infiltrating (intramuscular) lipoma, two benign but locally aggressive lesions, have been described in a variety of muscles throughout the body. A review of the literature has failed to disclose a case in which both of these lesions occurred within the same muscle. The following report describes the simultaneous occurrence of these two lesions within the gastrocnemius muscle of a middle-aged man.

CASE REPORT

A 48-year-old man presented with an enlarging right calf mass of one and one half years duration. He first developed a mass in the right calf in 1978. Because of increasing size of the mass an angiogram was performed in 1980; a circumscribed, nonvascular, soft-tissue lesion was identified in the gastrocnemius-soleus region. The lesion was subsequently resected and was found to measure 3.8 × 2.6 cm. While it was encapsulated on one surface, no distinct tissue plane was found on the other surface. On microscopic examination, stromal elements were found to be composed of fibroblast-like nuclei arranged in a plexiform pattern. The tumor was described as being well circumscribed.

The patient was asymptomatic until 18 months prior to this admission when he began to notice an enlarging mass in the posterior right calf and a tingling sensation in the same area after prolonged walking. The patient had a history of a right Achilles tendon rupture 16 years prior to admission and a right ankle fracture 15 years prior to admission.

FIGURE 1. Posterior view of mass in right calf.

The physical examination was unremarkable except for a fist-sized, firm, nontender mass in the posterior right calf (Fig 1). The gastrocnemius muscle proximal to the mass was soft. The patient had a normal gait pattern and normal strength in the right gastrocnemius-soleus mechanism. Computed tomographic (CT) scan (Fig 2) showed the gastrocnemius muscle to be replaced by fatty tissue with well-preserved fascial planes. In addition, there was an area of dense tissue within the low density lesion. An angiogram of the right calf demonstrated a lobulated soft tissue mass with moderate tumor vascularity derived primarily from the posterior tibial artery (Fig 3). The external iliac, common femoral, superficial deep femoral, and popliteal arteries were normal.

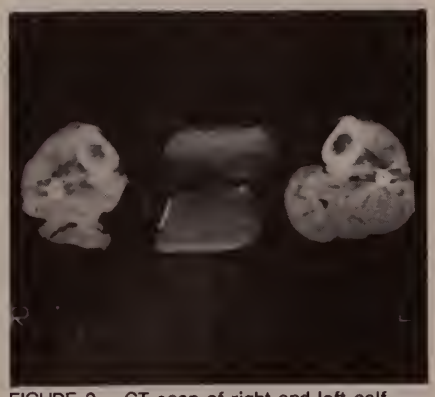

FIGURE 2. CT scan of right and left calf.

The patient underwent block resection of the tumor with removal of the entire gastrocnemius muscle and the medial half of the soleus muscle. The neurovascular structures could be separated from the region of

FIGURE 3. Angiogram of right calf lesion.

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FIGURE 4. Resected specimen; arrows indicate the fibromatosis.

resection and were preserved. The postoperative course was uneventful and the wound healed by primary intention.

The surgical specimen consisted of the entire gastrocnemius muscle, a portion of the soleus muscle, and the overlying skin and connective tissue. The portion of the soleus muscle was grossly normal in appearance. A longitudinal section of the gastrocnemius muscle (Fig 4) demonstrated a thin peripheral rim of normal striated muscle measuring up to 0.8 cm in thickness situated along the posterior aspect of the gastrocnemius. The remainder of the muscle was composed of soft, light yellow striated tissue that could be seen to gradually merge with the thin strip of normal muscle. A firm, nonencapsulated, lobulated, white fibrous mass measuring 2.5 cm in its greatest dimensions arose from the fascia of the muscle and was situated within the yellow striated tissue.

Microscopic examination of sections from the fibrous mass revealed elongated spindle-shaped fibrocytes separated by collagen and arranged in sweeping bundles. None of the cells had atypical or hyperchromatic nuclei. Mitotic figures were also absent (Fig 5).

Microscopic examination of the yellow striated tissue revealed well-differentiated lipocytes separating striated muscle cells (Fig 6). Many of the muscle cells showed atrophic changes. The lipocytes were mature cells with peripheral nuclei; no lipoblasts or atypical cells were present.

Discussion

Extra-abdominal fibromatosis is a benign proliferation of fibrous tissue that arises from the connective tissue of the muscle and the overlying fascia or aponeurosis.[2,5] The cause of this proliferation is uncertain. The lesion is seen most often between puberty and 40 years of age with the peak incidence occurring between 25 and 35 years of age. Both men and women are equally affected. The most common sites of fibromatosis are the shoulder and pelvic girdles, the thigh, and the lower leg. The usual presentation is that of an enlarging mass with or without pain. When neural elements are involved pain is present.

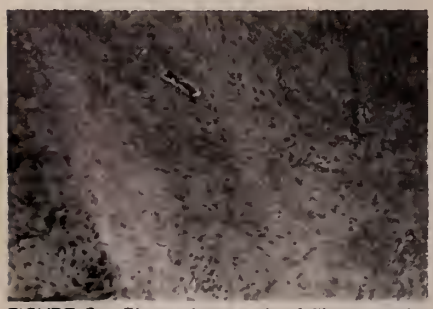

FIGURE 5. Photomicrograph of fibromatosis. (Hematoxylin and eosin stain; original magnification × 63.)

The tumors of fibromatosis are nonencapsulated and have a hard, rubbery consistency. Cut surface reveals glistening, pink-white fibrous tissue. Microscopically the lesion is composed of uniform, mature fibrocytes separated by collagen bundles. Mitoses are rare and atypical cells are absent. It is important to differentiate this lesion from fibrosarcoma. The latter has a high degree of cellularity, a greater number of mitoses along with atypical mitoses, tumor giant cells, and a greater variation in size, shape, and staining characteristics of the cells.[3] Fibromatosis is locally aggressive but does not metastasize. This lack of metastases led Stout[7] to regard these tumors as a separate clinicopathologic entity distinct from fibrosarcoma, as he felt that the designation "sarcoma" should be reserved for mesenchymal neoplasms with a metastatic potential. Because fibromatosis is locally invasive, a few pathologists feel that it should be considered a low-grade fibrosarcoma. However, Stout's concept of fibromatosis is almost universally accepted.[2] The treatment of choice is complete excision. Reported recurrence rates vary from 25 to 65%.

Infiltrating or intramuscular lipoma is a benign lesion of mature lipocytes that infiltrates between striated muscle fibers.[4] It usually affects the large muscles of the extremities. It occurs more often in men and usually between 30 and 60 years of age. The usual presentation is that of a slow-growing, painless mass. Cross section of the lesion reveals yellow adipose tissue gradually replacing the muscle and possibly extending beyond the fascia of the muscle. The cut surface often has a striated appearance due to the proliferation of fat cells between the muscle fibers. Microscopic examination shows mature lipocytes with peripheral nuclei infiltrating the muscle. The entrapped muscle cells show atrophic changes. No lipoblasts or atypical cells are seen and this serves to differentiate this lesion from a well-differentiated liposarcoma. The intramuscular lipoma has a tendency to recur if

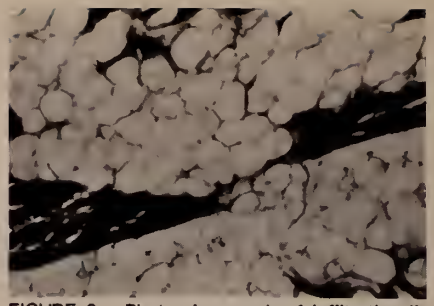

FIGURE 6. Photomicrograph of infiltrating lipoma. Note striated muscle fibers infiltrated by mature lipocytes. (Hematoxylin and eosin stain; original magnification × 100.)

not completely excised. The prognosis is excellent if complete excision is possible.[2,9-12]

Considerable amounts of nonneoplastic adipose tissue may accumulate between muscle fibers in atrophy caused by muscle disuse or denervation, resulting in a histologic picture quite similar to that of infiltrating lipoma. Neither atrophy nor denervation appears to be a factor in the present case; the recovery from the ruptured Achilles tendon many years earlier was without incident, and the patient was physically active until the time of the current surgery. Also, the atrophy of disuse would be expected to affect all of the musculature of an unused extremity, not just a single muscle.

This case illustrates the simultaneous occurrence of an extraabdominal fibromatosis and intramuscular lipoma within one muscle. To the best knowledge of the authors, this is the first such case reported in the literature. The fibromatosis was a recurrence of a tumor resected five years earlier. Block excision, the treatment of choice for both lesions, was performed. Due to the locally aggressive nature and high rate of recurrence of both lesions, close follow-up is indicated.

Acknowledgment. The authors thank Ms Lillian Aquino and Ms Jacquelyn Green-Hill for their assistance in manuscript preparation.

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Adenovirus pericarditis

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Adenovirus causes approximately 7% of all childhood respiratory tract diseases,[1] that vary in severity from simple coryzal episodes to invasive pulmonary disease.[2] Adenovirus infection outside of the respiratory tract may involve the pericardium, myocardium, liver, pancreas, kidney, bladder, central nervous system, and skin.[3] However, there is a paucity of information in the literature on pericarditis due to adenovirus. We recently cared for a child with adenovirus pneumonia and pericarditis and report her case to emphasize the presentation, diagnosis, and management of adenovirus pericarditis, as well as to review the relevant literature.

Case Report

A 15-month-old girl with Down's syndrome developed rhinorrhea, progressive lethargy, and anorexia two days prior to admission to Nassau County Medical Center. In the emergency room a diagnosis of upper respiratory tract infection and pneumonia was made; amoxicillin, decongestants, and antipyretics were prescribed. The patient returned the next day and was admitted to the hospital because of fever, mild respiratory distress, and postprandial vomiting. Her temperature was 38.2°C rectally; pulse, 156 beats/min; respirations, 40/min; blood pressure, 100/60 mm Hg; and her weight was 6.4 kg.

Physical examination revealed an undernourished hypotonic child with clinical features typical of Down's syndrome. A profuse mucopurulent nasal discharge, enlarged tonsils without exudate, bilateral coarse rales, and a liver edge palpable 1 cm below the right costal margin were found. Heart sounds were normal, and no pericardial friction rub was heard.

The hemoglobin level was 11.7 g/dL; hematocrit, 34.1%; WBC count, 18,500/μL with 55% neutrophils, 21% bands, 19% lymphocytes, and 5% monocytes; and platelet count, 296,000/μL. The erythrocyte sedimentation rate was 39 mm/h, and serum cold agglutinins were not present. Blood urea nitrogen, serum creatinine, aspartate aminotransferase (SGOT), alanine aminotransferase (SGPT), amylase, and ammonia determinations were within normal limits. There was 1+ protein on urine analysis and a Mantoux skin test was negative. An initial chest roentgenogram revealed a right upper lobe infiltrate and a normal cardiac shadow. Blood cultures obtained on admission and 48 and 72 hours later were sterile. Urine was negative for *Hemophilus influenzae* type B, *Neisseria meningitidis* A, B, C, Y, and W-135, and *Streptococcus pneumoniae* antigens by latex agglutination.

The patient was initially treated for suspected bacterial pneumonia with intravenous ampicillin 150 mg/kg/d. Loose stools developed on the second hospital day and she remained febrile but without signs of respiratory distress until the fourth hospital day when she began to sleep more than usual, refuse oral feedings, and develop pallor, nasal flaring, and subcostal retractions. Her pulse was 148 beats/min and blood pressure was 84/60 mm Hg. Heart sounds were muffled and the liver edge was still palpable 1 cm below the right costal margin. No pericardial friction rub was heard. An arterial blood gas on room air revealed a pH of 7.41, P_{O_2}, 62 mm Hg, and P_{CO_2}, 43 mm Hg. Chest roentgenogram (Figure) revealed marked cardiomegaly and an increase in the

FIGURE. A right upper lobe infiltrate is present, and the heart is enlarged and globular in configuration. The cardiac silhouette was normal on admission.

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right upper lobe infiltrate. Low voltage QRS complexes and flat T waves were seen on the limb and precordial leads of an electrocardiogram and a two-dimensional cardiac ultrasound demonstrated a moderate pericardial effusion. Viral cultures collected from the nasopharynx, throat, and rectum on admission were reported to be growing adenovirus that was later determined to be type 7. Although a presumptive diagnosis of adenovirus pneumonia and pericarditis was made, antibiotic therapy was changed to oral trimethoprim-sulfamethoxazole for seven days for possible pulmonary bacterial superinfection.

Because the patient demonstrated clinical improvement throughout the day, it was decided to perform a pericardiocentesis only if cardiovascular compromise ensued or if the original diagnosis became questionable. She continued to improve clinically and was discharged on the tenth hospital day.

Complement-fixing antibody titers to adenovirus group antigen rose from <4 to 16 in serum specimens drawn two weeks apart. No titer rise was demonstrated for influenza A and B, parainfluenza 1 and 3, or mycoplasma. The patient was well at visits to the clinic one and two months later; repeat chest roentgenogram and echocardiogram revealed complete resolution of the pneumonia and pericardial effusion.

Discussion

Adenovirus causes less than 10% of pneumonia in children but type 7, the etiologic agent in 46% of 168 cases of adenovirus pneumonia, was associated with a 20% case fatality rate in a recent 25-year review of the literature.[4] Pericarditis, on the other hand, is a relatively rare complication of invasive adenovirus disease with only four previously published examples.[3,5-7]

Johnson and associates reported the first such association between type 3 adenovirus infection and clinical pericarditis in a 22-year-old man with serologic evidence of infection.[5] Nahmias and coworkers isolated adenovirus type 7 from the pericardial fluid of a 10-month-old girl who died from severe pneumonia and acute pericarditis.[6] Van Reken and associates also reported isolation of adenovirus type 7 from pericardial fluid and serologic confirmation by complement fixation in a 4-year-old girl with a presentation similar to our patient's.[7] Odio and colleagues recently described a case of disseminated adenovirus infection in a 2-year-old girl with multi-organ involvement, including the lower respiratory tract and pericardium.[3] Adenovirus complement fixation titers were positive but viral cultures from multiple sites were negative.

The recrudescence of respiratory distress in our patient being treated for pneumonia prompted us to repeat the chest roentgenogram that revealed the new findings of cardiomegaly. Electrocardiogram and echocardiogram then confirmed the presence of a pericardial effusion. Pericardiocentesis was not performed because the patient's clinical status improved and the positive adenovirus culture results became known. Seroconversion of complement fixation antibody titers to adenovirus later confirmed an acute adenoviral infection. Although pericardial fluid was not available for examination and culture to confirm the presence of virus or to exclude a bacterial process, the empiric antimicrobial regimen this patient received for bacterial pneumonia would have been unlikely to cure a purulent bacterial pericarditis without the surgical drainage warranted for this entity.[8] Our experience serves to remind the pediatrician that pericarditis may complicate common infections due to adenovirus and other viruses as well.[9]

Signs and symptoms of acute viral pericarditis with effusion depend on the agent involved; however, an upper respiratory tract infection commonly precedes the illness.[10] The young infant may present with respiratory distress characterized by pallor, cyanosis, shortness of breath, and difficulty in feeding. In the older child, more specific complaints such as chest pain, cough, dyspnea, and fatigue may be more prominent. Although viral pericarditis generally responds to conservative medical management, pericardiocentesis is indicated when cardiac tamponade occurs or when the diagnosis is questionable.[11]

Acknowledgment. The authors thank Dov Nudel, MD, for his suggestions.

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This section is designed to offer rapid publication (usually within 1-3 months) of new clinical, epidemiologic, and laboratory observations, as well as of comments on articles published in the Journal *or on any topic related to the role of the physician. Letters should be typed double-spaced and should include the professional affiliation, highest academic degree, address, and signature of each author. Preference is given to letters not exceeding 450 words. All letters are personally reviewed and acknowledged by the Editor. Address correspondence to Editor,* New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042.*

On being a child with short stature in a taller world

TO THE EDITOR: In their recent article entitled, "The child with short stature" (1986, 86:15-21), Drs Oberfield and Levine correctly refer to the "significant physical and social embarrassment" that many short children (and their parents) suffer because of their comparative lack of body size. The damaging impact on self esteem and the emotional hurt caused by frequent calls of "shrimp," "midget," and "peanut" are well known and do not require further elaboration.

Less well known and rarely mentioned is another side of the issue. There is historic-psychologic evidence that, in many cases, points to a possible correlation, at times even a close connection, between physical shortness and the development of amazing feats of creativity. Few people seem to be aware of the fact that Pablo Picasso, perhaps the best known artist of our century, never grew beyond 5′2″ in height; that John Keats and Somerset Maughan were short people (approximately 5′3″); that Vladimir Gogol, one of the greatest Russian writers, was a man of distinctly diminutive body size, and that during childhood his schoolmates called him "the mysterious dwarf." Gustave Eiffel, the builder of the tower with the same name in Paris, was short and stooped. Regarding contemporary famous Frenchmen, Jean-Paul Sartre and Raymond Aron were able to transmute their bodily "short"-comings into towering intellectual achievements. So did Napoleon in the political and military field. The German philosophers Moses Mendelsohn and Emanual Kant were of diminutive body size and the "shortest" philosophers in their day teaching at the Universities of Berlin and Konigsberg.

Several of my own "short" patients stated that their success in art and science was in part a result of their intense desire to compensate for their small bodies.

Toulouse-Lautrec, the crippled dwarf whose masterworks were recently exhibited at the Museum of Modern Art, stated it all in one brief sentence: "If my legs had been a little longer, I should never have painted."

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Metastatic breast carcinoma presenting as acute appendicitis

TO THE EDITOR: The potential for breast carcinoma to produce widespread metastases predisposing to a variety of clinical manifestations is well documented. Appendiceal metastasis is rare and has to our knowledge not been reported even though gastrointestinal involvement is common.[1-3]

Case Report. A 60-year-old woman was admitted to the hospital with an acute abdomen that later required surgical intervention. A mastectomy performed five years earlier revealed infiltrating ductal carcinoma that had metastasized to the internal mammary and axillary nodes.

The appendix was removed; on examination it was covered by fibrinopurulent material. Microscopic examination revealed neoplastic cells with predominant areas of squamous differentiation and other areas showing gland formation. A review of the primary tumor removed five years earlier showed infiltrating ductal carcinoma with large areas of sarcomatoid and squamous differentiation. It is interesting to note that metastases from such a lesion may present as a pure or almost pure squamous cell carcinoma, as in this case.[4]

Discussion. Secondary neoplasia of the bowel is rare. The incidence of gastrointestinal metastasis from the breast has been reported to be 16.4% of all breast carcinoma cases.[5] The most frequent sites of metastasis have been the stomach and the small intestine. Large intestinal metastases occur less frequently and appendiceal metastasis has not been reported previously in the literature reviewed.[2,3]

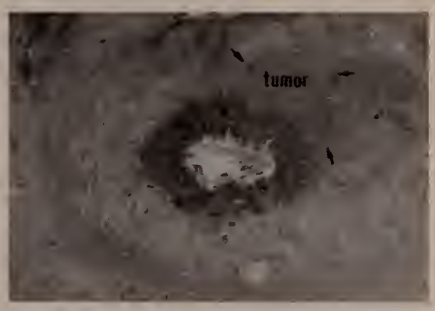

FIGURE. Scanning view of the appendix showing an uninvolved mucosa and tumor in the submucosa and muscular layer.

Appendiceal metastasis from the breast probably occurs as an embolic phenomena. In our case, the neoplasm was located primarily in the submucosa and was not found to involve the mucosa (Figure).

Obstruction of the small appendiceal lumen predisposes to acute inflammation and even perforation. Secondary and even primary tumors—predominantly carcinoids and carcinomas—could easily cause obliteration of the lumen with subsequent development of appendicitis, which is its most common clinical presentation.[6,7]

Clinical manifestations of gastrointestinal metastasis are varied and the possibility of metastatic disease should always be considered in patients with known breast carcinoma who develop acute abdominal symptoms.

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The use of a breathing maneuver in the physical diagnosis of angina

TO THE EDITOR: Chest pain is a common phenomenon in patients both with and without cardiac problems. Current diagnostic methods in cardiology rely on modern technologic advances and place less dependence on clinical physical diagnosis.

I have found the maneuver of controlled inhalation and exhalation helpful in the differential diagnosis of patients complaining of chest pain. Discomfort in the chest may be conveniently divided into four broad categories: muscular-skeletal-fibrotic, pleuritic, pulmonic, and cardiac. Cessation of chest motion tends to eliminate the first three categories, leaving only cardiac involvement (generally) while excluding pericarditis. W. Proctor Harvey, MD, Professor of Medicine at Georgetown University Hospital stated that he is familiar with the maneuver, although unable to cite specific published references (personal communication, May 22, 1985). Alfred Soffer, MD, Editor-in-Chief of *Chest*, relates that he has used the same maneuver in physical diagnosis, particularly to distinguish between angina pectoris and pleuritic disease. However, he also is unable to recall a published article on the subject (personal communication, April 11, 1985).

A review of 379 citations from 1979 to 1985 under the heading "Diagnosis of Angina Pectoris" from the Bibliographic Citation List generated by the National Interactive Retrieval Service of the National Library of Medicine revealed no reference to the breathing maneuver.

Angina pectoris is a clinical diagnosis. Objective examinations such as coronary arteriography and exercise electrocardiograms may aid in assessing the underlying pathologic conditions responsible for the pain and in evaluating the functional status and prognosis of patients. However, the diagnosis ultimately rests on the physician's clinical judgment.[1]

Shub[2] notes that chest pain may be affected by deep breathing or chest motion. Harrison[3] wrote that after 30 years of observation more than 60% of patients with undoubted angina pectoris also have other causes of chest or shoulder girdle pain.

Hickam[4] described a clinical rule for classifying possible anginal syndrome. Pain brought on by a deep breath received a coefficient of −2. The coefficient levels ranged from −2 indicating a low probability of angina to +2 indicating a good probability of angina.

The pain associated with pericarditis is believed to be due to inflammation of the adjacent parietal pleura. Pericarditis causes two distinct types of pain. By far the most common is the pleuritic pain related to respiratory movement and aggravated by cough and deep respiration. The next common type of pericardial pain is the steady, crushing substernal pain that mimics that of acute myocardial infarction. Occasionally both types of pain may be present simultaneously.[5]

The public should be taught to recognize both anginal and nonanginal symptoms; pain that cannot be diagnosed as nonangina should be suspected as possible angina. There is a high frequency of chest pain in patients who have had sternal-splitting procedures for bypass surgery for several months following the procedure. Most frequently, the discomfort arises from body motion and expansion and contraction of the thorax. Patients in the rehabilitative period after sternum-splitting surgery, and even beyond, discover much to their amazement that on motion or exercise, whether ambulatory or stationary, there is onset of substernal discomfort or pain. Of course, a marked psychic response occurs. This may be allayed by the use of the breathing maneuver resulting in relief from fear, anxiety, and pain. This maneuver may be equally useful in patients suffering from chronic arthritis of the thorax and following fracture of the ribs.

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Hemorrhagic shock in amyloidosis of the urinary bladder

TO THE EDITOR: Reactive systemic amyloidosis (secondary systemic amyloidosis) is rare as a cause of bladder hemorrhage. However, it should be considered as a possibility because of the potential for massive and catastrophic vesical hemorrhage in patients suffering from certain chronic diseases.[1,2]

There have been 49 reported cases of vesical amyloidosis in the literature.[3-6] To our knowledge, only eight of these cases have been due to reactive systemic amyloidosis. This disorder is caused by an acute recurrent and chronic infectious, inflammatory, or nonimmunocyte-derived dyscrasia or neoplastic disease.[1,2]

Case Report. A 68-year-old woman presented in shock to the emergency ward. Gross hematuria that had started 11 hours earlier was associated with abdominal pain and fainting. On physical examination, her blood pressure was 55/40 mm Hg, and the pulse rate was 116/min. A few moist rales were heard over the left lower chest and a mass in the lower abdomen extending to the umbilicus was noted. Her medical history was significant for rheumatoid arthritis for more than 20 years and a left phreniclasia in 1947 for the treatment of presently inactive pulmonary tuberculosis. These were well documented in the records of previous hospitalizations.

Following emergency measures, an excretory urography and cystogram were obtained. The renal outlines were poorly visualized but intact. The bladder appeared large with many ill-defined filling defects (Fig 1). A chest radiograph revealed density at the left base presumably due to fibrosis (Fig 2).

FIGURE 1. Excretory urogram and cystogram showing poor visualization of kidneys and a distended bladder with ill-defined filling defects.

FIGURE 2. Chest radiograph showing density at left lower base and fibrosis.

Laboratory data showed a hemoglobin of 7.1 g; hematocrit, 21.8%; and BUN, 32 mg%. Routine urine cultures and sputum and urine cultures for acid-fast bacilli were negative. Urinary cytology was benign. Intravenous fluids and blood transfusions (a total of 10 units) were started immediately. Aggressive manual irrigation proved unsuccessful in evacuating the bladder. Endoscopic evaluations with evacuation of clots and fulguration of the bleeding points were performed on the 1st, 4th, and 14th days of hospitalization. The bladder was filled with pseudo-organized laminated and adherent clots. A resectoscope with cold loop was frequently used to break up the clots. The vesical urothelium appeared denuded with linear and punctate oozing points. The trigone was uninvolved.

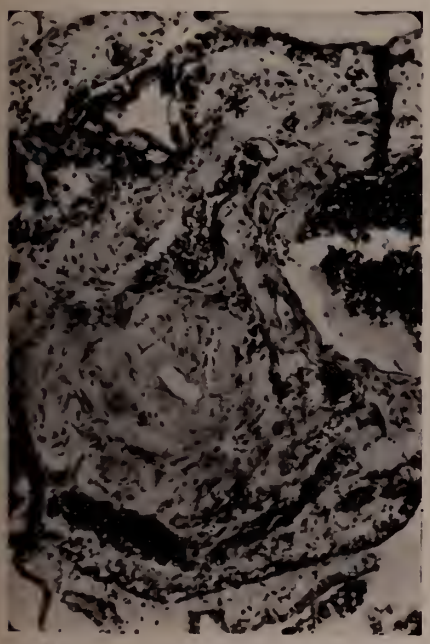

FIGURE 3. Vascular amyloid deposits as seen in microscopic preparations of bladder biopsy. (Hematoxylin and eosin stain; original magnification × 400.)

A bladder biopsy made the diagnosis of amyloidosis definitive. The biopsy specimen revealed vascular amyloid deposits (Fig 3) that appeared lime-colored when stained with Congo-red and viewed with the polarizing light. A sigmoidoscopy with rectal biopsy demonstrated amyloidosis and proved the systemic nature of the disease. In our case, conservative therapy was successful. The BUN and creatinine were stable 20 months later. The urinary sediment contained a few fine granular casts without significant pyuria or bacteria.

Discussion. A grave prognosis associated with vesical hemorrhage in reactive systemic amyloidosis has been reported.[6] At times, biopsy has triggered massive and catastrophic bleeding.[4-7] Progressive deterioration and necrosis of the bladder wall has also been observed.[3]

Reactive systemic amyloidosis is a rare cause of massive hematuria. However, with a 14 to 26% incidence of reactive systemic amyloidosis in patients with rheumatoid arthritis, and a high incidence in patients with tuberculosis and certain chronic diseases, it deserves consideration as a possible cause of hematuria of undetermined etiology.

The diagnosis of amyloidosis may be established by noninvasive methods or by biopsy.[1,2] Conservative management is preferred; if conservative means are not effective then cystostomy, bilateral ureteral catheterization, and ligation of the hypogastric arteries may be necessary. Hematuria, in association with a number of diseases, should suggest reactive systemic amyloidosis as a possible cause. These diseases include rheumatoid arthritis, juvenile chronic polyarthritis, psoriatic arthritis, ankylosing spondylitis, Reiter's syndrome, chronic rheumatoid heart disease, dermatomyositis, scleroderma, tuberculosis, leprosy, chronic pyelonephritis, chronically infected decubitus ulcers and burns, osteomyelitis, syphilis, ulcerative colitis, regional ileitis, malaria, and Hodgkin's disease.

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The need for physician involvement in politics

TO THE EDITOR: Our political action committees have attempted to influence the direction of state legislation by means of political contributions to those legislators who supported positions taken by the Medical Society of the State of New York. To my way of thinking, political action means more than simply writing the biggest possible check to politicians; rather we need as physicians to be truly politically active.

As physicians we represent a limited constituency and a limited number of votes. We need to be far more active in the political process itself. I hold a minor political office as a village trustee. As an elected public official, I not only represent a constituency of my colleagues, but also of the voters who put me into office. Now when I speak with my state senator and assemblyman, they listen to me not just as a physician but as an elected public official. We need more physicians to be active within the political process and not just as mere observers sending occasional contributions.

In summary, I think that the entire thrust of our political action committees has been misdirected. Local communities have many offices, both elective and nonelective, in which physicians could serve. Only by working within the system will we be able to make needed changes. The lawyers learned this a long time ago.

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In reply. I fully agree with the general content of Dr Horey's letter. Article II of the bylaws of the New York Medical Political Action Committee (NYMPAC), and particularly the first three

items of Article II, covers the points stressed in his letter.

Article II: Purpose

1. To promote and strive for the improvement of government by encouraging and stimulating physicians and others to take a more active and effective part in governmental affairs.
2. To encourage physicians and others to understand the nature and actions of their government as to important political issues, and as to records of incumbents and candidates for elective office.
3. To assist physicians and others in organizing for more effective political education and political action in carrying out their civic responsibilities.
4. To participate in raising revenue, endorsing, and financially supporting those political principles and candidates for public office who best represent the principles of the medical profession and the interest of those it serves.

Unfortunately not all physicians are either able or willing for a variety of reasons to become candidates for political office. Consequently, Section 4 of Article II assumes great importance.

Under Article IV: Allocation of Funds, all contributions are to be divided into three accounts: Operating, State Political Action, and Federal Political Action. The article goes on to state that up to 25% of the total contributions to NYMPAC may be allocated to the Operating Account (ie, political education among other things), and the remainder is to be divided with two thirds going to the State Political Action Account and one third to the Federal Political Action Account. It is possible to obtain funds from these accounts by application to NYMPAC based on contributions of our county members. As a practical matter local participation must be sufficient to warrant application for funds via this route. Too often membership figures are 10% or less.

Although I have not personally sought elective political office, I have been a member and am currently chairman of the Planning and Zoning Commission of the City of Corning. Recently I suggested to the Executive Committee and the members of the Steuben County Medical Society that monetary contributions be made through NYMPAC rather than to individual political candidates. This will enable organized medicine to speak more effectively with one voice.

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FROM THE LIBRARY

ON POLITICS AS A FIELD OF USEFULNESS FOR THE PHYSICIAN

Every physician has been advised to keep out of politics. This advice cannot be escaped. The commencement-day orator hands it out to the graduating class, the old physician cautions the young man against "mixing in politics," the literature of medicine perpetrates the admonition, and medical circles have a perennial sneer for the "political doctor." We earnestly wish that there might be less of this sentiment. It is neither fair to the State nor to the medical profession: it deprives the former of the interest of its best class of citizens and the latter of the advantages of availing itself of the opportunities of self-government. To advise any class of citizens to abstain from politics is to advise self-defranchisement.

Politics is the science and practice of government. It is "clean" or "dirty," as the people who participate are clean or dirty. No class-day orators are advising the dive-keeper or the man who preys upon the lives and property of the people to keep out of politics; as a matter of fact he is strictly in it, and has more legislation influenced in his interest and places more of his friends in office in one year than the medical profession does in ten years. This is partly due to class-day oratory.

The science of medicine has brought about as far as it can the solution of the tuberculosis problem and the typhoid fever problem and a host of other similar problems which are as vital to the people as are the lives of their children, and in fact they are the same. Medicine has shown how these diseases may be exterminated. Now these matters are up to the State. That means their further development is in the hands of politics. And shall our profession, after having hunted down the monster of typhoid, and gotten it at bay in its lair, cowed and at our mercy, desist from having the *coup de grace* because the stroke must be applied with the bloody lance of politics? We need more doctors in our legislative chambers and in our executive offices. Medicine has long ago grown past the function of administering to those who perchance have fallen sick. It has become the most salutary department in the commonwealth, and we are not raising up men fast enough to administer its new offices. We may justly be accused of slothfulness in our duty to the people.

Observations
(*NY State J Med* 1907; 7:460)

Maimonides' Medical Writings: Volume I. Treatises on Poisons, Hemorrhoids, Cohabitation

Translated and annotated by Fred Rosner, MD. 185 pp, Haifa, Israel, The Maimonides Research Institute, 1984 (hardcover)

The 850th anniversary of Maimonides' birth was celebrated in 1985. Moses Maimonides (Abū Imrâm Mûsâ Ibn Maimûn in Arabic) was born into a distinguished family in 1135 (Hebrew year 4895) in Cordova, Spain. His mother died in childbirth and he was essentially raised by his father who was a judge (*dayan*). Although Cordova was an Islamic city, its citizens, including the Jews, were given a large measure of religious freedom. This abruptly changed, however, in 1148, when the city was captured by the followers of a fanatical Islamic sect, the Almoravids (Al-Murābitīn), the "unitarians." Maimonides was 13-years-old at the time. His family remained in Cordova for some time, practicing Judaism in private while appearing as Moslems in public.

The Almoravids were essentially an Islamic reform movement of proselytization and military conquest that affected the western Sahara, Sahel, Maghreb, and Iberian peninsula. It was because of the movement's fanatical nature and rigid intolerance that the Maimons were eventually forced to leave Cordova. In view of the importance of this movement on where Maimonides eventually came to settle, it is worthwhile giving it some consideration. This movement and the *jihad* it produced sprang up in southern Morocco and first spread to sub-Sahara West Africa. Its originator was Abdallah ibn Yācine who was a teacher at an Islamic school known as the Dar al-Murābitīn.[1] Abdallah was invited by the Chief of the Jeddala, a Sanhaja Berber group, Yahyā ibn Ibrāhīm, to preach to his people. Ibrāhīm had come into contact with Abdallah on his return from a pilgrimage to Mecca in 1035/36. Abdallah imposed rigorous Islamic law on the Jeddala under which they chafed and after Ibrāhīm's death they drove him out. As before and since, Abdallah, like all potential jihadists, escaped to a *ribat* (religious retreat). In 1040 he chose one on the Senegal River near present day Podor. There he and a handful of followers enjoyed the protection of the Tekrur ruler, War Jabi.

Abdallah made many converts along the river and most importantly converted the Lamtuna Arabs who became the core of the movement. Within two years he had converted many of the Saharan tribes to his cause and then moved to capture the key towns of the western trans-Saharan trade route, Sijilmasa and Audaghast. This had an immediate effect on the African empire of Ghana, whose gold and slaves moved north along this route in exchange for Mediterranean goods. Abdallah's remarkable progress was in large measure sustained by the military genius of the Lamtuna chiefs, Yahyā ibn 'Umar and Abū Bakr ibn 'Umar. Abdallah was killed in 1059 in a battle against the Barghawata; Abū Bakr ibn 'Umar then became leader of the Almoravids.[2]

Although deprived of the leadership of its original religious founder, the movement gained momentum under Abū Bakr. Leaving his cousin, Youssof ibn Tāchfīne in the north, he went south to put down a rebellion among the Sanhaja. Youssof, now ensconced in the north, refused to yield his position on Abū Bakr's return. Eventually a compromise was agreed on, with Abū Bakr assuming leadership in the south and Youssof in the north.[3]

In 1076 Abū Bakr invaded the animist black African Empire of Ghana, effectively destroyed it and installed a converted ruler. In 1087 when Abū Bakr died Ghana received some respite because the Sanhaja of the desert became fragmented and engaged in internecine warfare. The Almoravid movement eventually faded away south of the Sahara, but it left behind a legacy of converted rulers and nobles in Tekrur and Ghana and large numbers of superficially converted Africans. The destruction of the Ghana Empire left a political void that fostered the emergence of the Mali Empire.[4]

In 1059, the year that Abdallah, the founder of the movement was killed, the Maimon family moved to Fez in Morocco. During the previous 11 years, since the Almoravid conquest of Cordova, Maimonides had continued his Judaic and scientific studies. Although Fez was under the control of the Almoravids, the Maimons were better able to disguise themselves since they were strangers in the city. In Fez, Maimonides continued his Judaic studies, and he also studied Greek philosophy. In 1165 the Maimon family left Fez in response to the execution of Rabbi Judah ibn Shoshan, with whom Maimonides had studied.

The family then went to Palestine, but due to a poor local economy moved to Egypt where they settled in Fostat, near Cairo. Several twists of fate then led Maimonides to practice medicine. His father died shortly after their arrival in Egypt and his brother, David, who was a jewelry merchant and the main support of the family, died in a shipwreck. Maimonides was now the sole support of an extended family, something he could not do through the practice of the rabbinate since it was then a public service freely given. For all of these reasons he turned to medicine; the remainder is well-known history. Maimonides

became a renowned physician, caring for the Sultan, Saladin, and for his successor, Al-Afdal. He maintained a large private practice, became a leading member of the Jewish community, and wrote extensively on diverse subjects.

The present volume under review here is the first of a series to be published by the Maimonides Research Institute in Haifa, Israel, on Maimonides' medical writings. It was sent to the reviewer by Ambassador and Mrs Meir Shamir. Currently the Israeli Ambassador to UNESCO, Ambassador Shamir served as the Israeli Ambassador to Mali during the time this reviewer served there for the US Public Health Service. The book is translated and annotated by Dr Fred Rosner who has already translated several of Maimonides' medical writings into English, and who has authored several books on Jewish medical ethics, medicine in Jewish law, and medicine in the Bible and the Talmud. He has brought to this work the required background of knowledge and the result is a volume that makes these medical writings of Maimonides, largely composed in the 12th century, accessible to 20th-century readers.

The book begins with a foreward by Rabbi Yehuda Assaf, Dean of the Maimonides Research Institute, who puts Maimonides' writings of 800 years ago into perspective when he says that they " . . . constitute a vivid exposition of the spiritual and ethical teachings of the Torah and a humble manifestation of God's perfect design of the universe and all living beings."

In the first chapter entitled, "The Medical Writings of Maimonides," Dr Rosner provides an insightful and informative overview of Maimonides' medical writings. These are placed into perspective against the background of the other numerous nonmedical works of Maimonides, including the *Mishna Torah* (*The Torah Reviewed*) that he completed in 1178 and considered his magnum opus. In 1191 he completed his classic on religious philosophy, *Dalālat al-ḥa'irīn* (*The Guide of the Perplexed*), known in Hebrew as *More Nevukhim*. These two works, in conjunction with his first book begun when he was 23-years-old entitled *Kitāb al-Sirāj* (*Commentary on the Mishna*), constitute a well-known trilogy.

Maimonides also wrote a number of other works and essays, many of them dealing with the problems faced at that time by the Jewish community. Maimonides also wrote the following ten medical works, as explained by Rosner in clear detail: *Extracts from Galen; Commentary on the Aphorisms of Hippocrates; Medical Aphorisms of Moses; Treatise on Hemorrhoids; Discourse on Asthma; Treatise on Cohabitation; Treatise on Poisons and their Antidotes; Regimen of Health; Discourse on the Explanation of Fits;* and *Glossary of Drug Names*. This latter work was only recently discovered in the Aya Sofia library in Istanbul as an Arabic manuscript. It was edited in Arabic by Meyerhof and then translated into French in 1940.[5] Muntner provided a Hebrew translation of the *Glossary of Drug Names* in 1969,[6] and it was subsequently translated into English by Rosner and published in 1979.[7]

It is clear from this list of writings, currently considered by scholars to be authentic works of Maimonides, that he covered a broad scope of subjects consisting of health in general and specific diseases in particular. Many of his works contain extracts from Greek medicine and they clearly demonstrate not only his extensive knowledge of the then extant Arabic medical literature, but also a familiarity with several languages. For example, Maimonides' earliest known work, *Treatise on Logical Terminology*, was written in Arabic.

Rosner appropriately points out that many researchers do not consider Maimonides' medical writings to be as original as his theological and philosophical ones. But what they lack in originality is more than compensated for in as Rosner says " . . . lucidity, conciseness and formidable powers of systematization and organization. . . ."

In this first volume, three of Maimonides' works are covered; the *Treatise on Poisons and their Antidotes*, the *Treatise on Hemorrhoids*, and the *Treatise on Cohabitation.* In so doing Rosner provides translations of relevant parts of these books, annotations, interpretations, analyses, and excellent background information about previous translations into different languages.

The section covering Maimonides' *Treatise on Poisons and their Antidotes* constitutes 94 of the book's 185 pages. It is divided into two sections, ten chapters, and an appendix. This work is the principal focus of Rosner's book; this is not surprising as it is without doubt one of Maimonides' most popular works. It covers a broad range of topics including snake bite, scorpion stings, animal bites, and injested poisons. During the Middle Ages this work was used as a standard textbook of toxicology. Some of the advice offered is still valid, such as tieing a ligature around a limb above the site of a snake bite and sucking out the "poison." This work was composed by Maimonides at the request of the Visier, Kadhi al Fadhil in 1198/99. Rosner provides a very valuable six and one half page summary and appreciation of this treatise, underscoring its high points and the current validity of some of the therapeutic measures described.

FIGURE. Bust of Maimonides. In the hall of the Jewish University of Jerusalem. From Krumbhaar EB: *A History of Medicine*. New York, Alfred A. Knopf, 1958, p 279, with permission.

The second work covered in this volume is the *Treatise on Hemorrhoids*. Originally written for a nobleman, possibly a member of the Sultan's family, its title does not accurately reflect its entire content. It contains detailed descriptions of the phases of digestion, the then accepted causes of hemorrhoids (usually black bile), and foods that were considered either harmful or beneficial to those with hemorrhoids. Remedies are then described in detail; some are still appropriate today.

The third work analyzed is the *Treatise on Cohabitation*. This is thought by many scholars to be one of Maimonides' earliest medical works, written in 1190/91 for the Sultan Hamat of Syria. Of all his medical works, the *Treatise on Cohabitation* attained the greatest reputation in Maimonides' lifetime. The Sultan was interested in increasing his sexual potency and thus this work with its euphemistic title essentially addresses this issue. Recipes of foods and drugs are provided, which are either aphrodisiac or antiaphrodisiac in their actions. Maimonides advised moderation in sexual intercourse, though it seems doubtful that the Sultan followed this advice. He died in 1192, a year or so after the *Treatise* was written. This work is a relatively short one, consisting of ten chapters. A longer version once thought to be authentic is now considered not to have been authored by Maimonides.

Although the various medical writings of Maimonides have been translated into different languages over the centuries, they continue to remain out of the reach of understanding for many. To fully appreciate them one must bring to their reading a knowledge of the historical times in which they were written, an understanding of the then current concepts of disease causation, and an awareness of antecedent medical thinking that influenced the therapeutic interventions of the day. *Maimonides' Medical Writings* serves as an insightful guide for both scholars and casual readers, taking them back over the centuries and through the intricacies of 12th-century medicine. The writings of Maimonides have flowered through the centuries because they embody an essential truth so well spoken by Alfred Lord Tennyson when he said "knowledge comes but wisdom lingers."

PASCAL JAMES IMPERATO, MD
Editor

1. Al Bakri: *Kitāb al-Masālik wa'l-mamālik*, in de Slane MG (trans): *Déscription de l'Afrique Septentrionale*. Alger, 1913.
2. Ibn Khaldūn: *Kitāb ta'rīkh al-duwal al-Islāmiya bi'l-Maghreb min Kitāb al-'Ibar*, in de Slane MG (trans): *Histoire des Berbères et des dynasties musulmanes de l'Afrique Septentrionale*. Paris, 1847, pp 238–239.
3. Ibn 'Idhārī al Marrākushī: 1306. *al-Bayān al-maghrib fī akhbār al-Andulus wa 'l-Maghrib*. In Miranda AH (ed): "Un Fragmento inedito de Ibn Idhari sobre las Almorávides": *Hespéris-Tamuda*. 1961, pp 58–59.
4. Imperato PJ: *Historical Dictionary of Mali*. ed 2. Metuchen, NJ, Scarecrow Press, 1986.
5. Meyerhof J: *Un Glossaire de Matière Médicale Composé par Maimonide (Sarh Asma al'Uggar)*. Cairo, Memorial Institute Egypte, 1940.
6. Muntner S, ben Maimon M: *Biyur Shaymoth Harefuoth (Lexicography of Drugs and Medical Responses)*. Jerusalem, Mossad Harav Kook, 1969.
7. Rosner F: *Moses Maimonides' Glossary of Drug Names*. Philadelphia, American Philosophical Society, 1979.

MSSNY Medical Liability Reform Fund Honor Roll

In the September 1985 issue the *Journal* began publishing the list of physicians who have generously contributed to the compaign to inform the public about the crisis in medical liability litigation. The names of additional contributors are listed below.

Gloria M. Allen, MD
Ralph Altman, MD
Dennis Barek, MD
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William Reid Pitts, Jr., MD
Allan Martin Rothenberg, MD
Steven Randy Rothstein, MD
Jonathan R. Schwartz, MD
Richard James Seeger, MD

ALLERGY

Psychobiological Aspects of Allergic Disorders. Edited by Stuart H. Young, MD, James M. Rubin, MD, and Harlan R. Daman, MD. 383 pp, illustrated. New York, Praeger Publishers, 1986. $37.95 (hardcover)

COMPUTER TECHNOLOGY

The Computer in Radiology. Edited by Tim B. Hunter, MD. 384 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1986. $39.95 (hardcover)

GERIATRICS

Practical Geriatric Therapeutics. By Richard W. Sloan, MD. 335 pp, illustrated. Oradell, NJ, Medical Economics Books, 1986. $24.95 (paperback)

Geriatric Medicine Annual 1986. Edited by Richard J. Ham, MD. 276 pp, illustrated. Oradell, NJ, Medical Economics Books, 1986. $32.95 (hardcover)

HEALTH CARE

The Home Health Care Solution. A Complete Consumer Guide. By Janet Zhun Nassif. 433 pp. New York, Harper and Row, 1985. $9.95 (paperback)

HISTORY OF MEDICINE

The Persisting Osler. Selected Transactions of the First Ten Years of the American Osler Society. Edited by Jeremiah A. Barondess, MD, John P. McGovern, MD, and Charles G. Roland, MD. 318 pp, illustrated. Baltimore, University Park Press, 1985. $45.00 (hardcover)

LABORATORY MEDICINE

The Office Practice Laboratory. By C. Robert Baisden, MD. 180 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1985. $29.00 (paperback)

MEDICAL EDUCATION

Implementing Problem-Based Medical Education. Lessons from Successful Innovations. By Arthur Kaufman, MD. 276 pp, illustrated. New York, Springer Publishing Co, 1985. $39.95 (hardcover)

MISCELLANEOUS

Dr Abravanel's Body Type Program. For Health, Fitness, and Nutrition. By Elliot D. Abravanel, MD, and Elizabeth A. King. 368 pp. New York, Bantam Books, 1985. $4.50 (paperback)

The Exercise Myth. A New Approach to Health and Fitness. By Henry A. Solomon, MD. 144 pp. New York, Bantam Books, 1986. $3.50 (paperback)

Marketing Strategies for Physicians. A Guide to Practice Growth. By Stephen W. Brown, PhD, and Andrew P. Morley, Jr, MD. 280 pp, illustrated. Oradell, NJ, Medical Economics Co, 1986. $27.95 (casebound)

Medical Acronyms and Abbreviations. By Marilyn Fuller Delong, RN. 328 pp. Oradell, NJ, Medical Economics Books, 1985. $10.95 (paperback)

Rusty's Story. The Dramatic True Story of One Woman's Triumphant Fight Against Illness. By Carol Gino. 342 pp. New York, Bantam Books, 1985. $3.95 (paperback)

We Are Not Alone: Learning to Live with Chronic Illness. By Sefra Kobrin Pitzele. 306 pp, illustrated. Minneapolis, MN, Thompson and Co, Inc, 1985. $14.95 (paperback)

OCCUPATIONAL MEDICINE

State of the Art Reviews. Occupational Medicine. The Microelectronics. Edited by Joseph LaDou, MD. 197 pp, illustrated. Philadelphia, Hanley and Belfus, Inc, 1986. $22.00 (hardcover)

ONCOLOGY

Cancer Risks and Prevention. Edited by M.P. Vessey, MD, and Muir Gray, MB. 301 pp, illustrated. New York, Oxford University Press, 1985. $29.95 (hardcover)

Tumor Markers: Clinical and Laboratory Studies. By Janis V. Klavins, MD. 214 pp, illustrated. New York, Alan R. Liss, Inc, 1985. $48.00 (hardcover)

ORTHOPEDIC SURGERY

Arthroscopic Surgery Update. Volume 5. Edited by John B. McGinty, MD. 153 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1985. $36.50 (hardcover)

Shoulder Surgery in the Athlete. Edited by Douglas W. Jackson, MD. 197 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1985. $36.50 (hardcover)

The Knee. Papers of the First Scientific Meeting of the Knee Society. Edited by Lawrence D. Dorr, MD. 143 pp, illustrated. Baltimore, MD, University Park Press, 1985. $40.00 (hardcover)

OTOLARYNGOLOGY

Practical Management of Eye, Ear, Nose, Mouth, and Throat Emergencies. Edited by Thomas O. Stair, MD. 183 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1986. $27.50 (hardcover)

PREVENTIVE MEDICINE

Maxcy-Rosenau Public Health and Preventive Medicine. 12th Edition. Edited by John M. Last, MD. 1,958 pp, illustrated. East Norwalk, CT, Appleton-Century-Crofts, 1986. $125.00 (hardcover)

PSYCHIATRY

Mental Disability in America Since World War II. By Don Martindale and Edith Martindale. 295 pp. New York, Philosophical Library, Inc, 1985. $15.00 (cloth)

Psychosomatic Illness Review. Edited by Wilfred Dorfman, MD, and Leo Cristofar. 215 pp. New York, Macmillan Publishing Co, 1985. $29.95 (hardcover)

RADIOLOGY

Clinical Computed Tomography. Illustrated Procedure Guide. By Lee C. Chiu, MD, James D. Lipcamon, RTR, and Victoria S. Yiu-Chiu, MD. 261 pp, illustrated. Rockville, MD, Aspen Publishing Co, 1986. $37.50 (hardcover)

Clinical Radiology of the Spine and Spinal Cord. By Mohamed Banna, MD. 449 pp, illustrated. Rockville, MD, Aspen Systems Corp, 1985. $78.00 (hardcover)

Oncologic Imaging. Edited by David G. Bragg, MD, Philip Rubin, MD, and James E. Youker, MD. 664 pp, illustrated. Elmsford, New York, Pergamon Press, Inc, 1985. $125.00 (hardcover)

Uniform warning label for aspirin

By June 5th, all nonprescription aspirin and aspirin-containing products must display a uniform warning label informing users about Reye's syndrome, according to a regulation issued by the Food and Drug Administration (FDA) in early March.

The uniform label, which was generally supported by most manufacturers, reads: "WARNING: Children and teen-agers should not use this medicine for chicken pox or flu symptoms before a doctor is consulted about Reye's syndrome, a rare but serious illness." The FDA issued the regulation on March 7; manufacturers have 90 days to comply.

The uniform warning will replace voluntary warnings some manufacturers of aspirin and aspirin-containing products have already included on product packages, said Health and Human Services Secretary Otis R. Bowen, MD. The new warning will bring consistency to the marketplace, and will enhance consumer understanding of the message, Bowen said.

Although the use of aspirin has not always been directly related to all cases of Reye's syndrome, studies have suggested that children and teen-agers who use aspirin for treating flu symptoms and chicken pox run a higher risk of developing the disease, according to a news release issued by the FDA. Reye's syndrome is a rare disease that is fatal in 20 to 30% of cases and may result in permanent brain damage.

The symptoms of Reye's syndrome are extreme fatigue, belligerence, and excessive vomiting. The symptoms tend to appear when a child or teen-ager seems to be recovering from the flu or chicken pox. Dr Bowen advises parents and teen-agers to be aware of the symptoms and "to get immediate hospital care, which can mean the difference between life and death when the symptoms are present."

Mayor appoints new health commissioner

Stephen C. Joseph, MD, assumed the position of Health Commissioner of New York City this month, after being appointed by Mayor Edward I. Koch in early March.

Dr Joseph replaced David J. Sencer, MD, who resigned from the post in January to take a position with a Boston consulting firm. Margaret T. Grossi, MD, had been acting health commissioner since Sencer's resignation.

Dr Joseph cited the acquired immune deficiency syndrome (AIDS) as the city's major health problem. He said he would work to reduce infant mortality, improve the city's environmental health, and improve access to health services for all New York City residents, including the homeless. It is unknown whether, in his efforts to deal with AIDS, Dr Joseph would support his predecessor's proposal to distribute hypodermic syringes to intravenous drug users in order to curtail the spread of AIDS. Mayor Koch rejected that proposal.

Dr Joseph left his position as special coordinator of the United Nations Children's Fund (UNICEF), an agency he joined in 1983, in order to take the health commissioner position. Prior to his work with UNICEF, Dr Joseph served as chief of pediatrics at Grenfell Regional Health Services in Newfoundland. He has also held positions at the Children's Hospital Center of the District of Columbia and with the Agency for International Development in central Africa.

Born in New York City in 1937, Dr Joseph received his medical degree from Yale University and his master of public health degree from Johns Hopkins University. He was a commissioned officer with the United States Public Health Service, serving as a Peace Corps physician in Nepal for two years.

In 1981, Dr Joseph resigned from his position as the highest-ranking health professional at the Agency for International Development in protest to a Reagan administration decision to oppose an order before the World Health Organization to ban the promotion of infant formula. The order was developed out of concern that such promotion of formula would discourage breast feeding.

AMA video clinic series appears on New York area cable program

The "Video Clinic," a series of one-hour programs produced by the American Medical Association now appears on the Lifetime Cable Television Network. The program is aired on Sundays at 1 PM and 10 PM, and Mondays at 3 AM, Eastern Standard Time.

The Video Clinic program distribution was expanded in April to include the Lifetime Cable Television Network and the Hospital Satellite Network. The expansion has permitted more than 400,000 physicians to view the educational series. The programs, produced at major national medical centers and featuring leading medical experts, are based on topics of interest to practicing physicians.

NEWS BRIEFS are compiled and written by Sandra Cirincione.

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Ernest Lovell Becker, MD, New York. Died February 21, 1986; age 63. He was a 1948 graduate of the University of Cincinnati College of Medicine. Dr Becker was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the Academy of Medicine, the American Physiological Society, the American Clinical and Climatological Association, the Society for Experimental Biology and Medicine, the American Society of Tropical Medicine and Hygiene, the New York County Medical Society, and the Medical Society of the State of New York.

David Franklin Brodey, MD, Brightwaters. Died February 9, 1986; age 79. Dr Brodey was a 1934 graduate of the University of Maryland School of Medicine, Baltimore. He was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Elizabeth Goodman, MD, Worcester, Massachusetts. Died February 10, 1986; age 82. She was a 1931 graduate of Boston University School of Medicine. Dr Goodman was a member of the Academy of Psychosomatic Medicine, the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

Eugen Grabscheid, MD, New York. Died February 3, 1986; age 82. He was a 1929 graduate of Medizinische Fakultät der Universität, Wien. Dr Grabscheid was a member of the New York Society of Laryngology and Otology, the New York Otological Society, the New York County Medical Society, and the Medical Society of the State of New York.

Anthony T. Graniero, MD, Utica. Died February 3, 1986; age 74. He was a 1950 graduate of Albany Medical College of Union University. Dr Graniero was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Surgery, and a member of the Academy of Medicine, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

John Roy Gregory, MD, Bronxville. Died February 19, 1986; age 67. He was a 1944 graduate of the University of Virginia School of Medicine, Charlottesville. Dr Gregory was a Fellow of the American College of Obstetricians and Gynecologists and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Academy of Medicine, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

William Steven Victor Gyves, MD, Bayside. Died February 23, 1986; age 66. Dr Gyves was a 1945 graduate of the New York Medical College, Flower and Fifth Avenue Hospital. He was a Diplomate of the American Board of Pediatrics and a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Francis F. Harrison, MD, Cooperstown. Died January 28, 1986; age 88. Dr Harrison was a 1925 graduate of Columbia University College of Physicians and Surgeons. Dr Harrison was a Fellow of the American College of Physicians, a Diplomate of the American Board of Internal Medicine, and a member of the American Association of Pathologists and Bacteriologists, the Medical Society of the County of Otsego, and the Medical Society of the State of New York.

Ralph C. Kahle, MD, Scarsdale. Died November 8, 1985; age 96. He was a 1920 graduate of Johns Hopkins University School of Medicine, Baltimore. Dr Kahle was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Orthopedic Surgery, and a member of the Academy of Medicine, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Adib H. Karam, MD, Akron, Ohio. Died December 29, 1985; age 82. Dr Karam was a 1930 graduate of Western Reserve University School of Medicine, Cleveland. Dr Karam was a member of the New York County Medical Society and the Medical Society of the State of New York.

Walter Keller, MD, Wadsworth. Died February 13, 1986; age 82. Dr Keller was a 1928 graduate of Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria. He was a member of the Medical Society of the County of Livingston and the Medical Society of the State of New York.

Leo Douglas Klauber, MD, Leonia, New Jersey. Died January 12, 1986; age 65. He was a 1945 graduate of New York Medical College, Flower and Fifth Avenue Hospital. Dr Klauber was a Fellow of the American College of Surgeons and a member of the Society of Surgical Oncology, the New York County Medical Society, and the Medical Society of the State of New York.

G. Charles LaBelle, MD, Whitesboro. Died February 3, 1986; age 82. He was a 1946 graduate of Albany Medical College of Union University. Dr LaBelle was a member of the Academy of Medicine, the American Geriatrics Society, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

Ely E. Lazarus, MD, New York. Died January 25, 1986; age 70. He was a 1939 graduate of New York University College of Medicine. Dr Lazarus was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Surgery. His memberships included the Academy of Medicine, the New York County Medical Society, and the Medical Society of the State of New York.

Vito Sebastian Lee, MD, Utica. Died January 29, 1986; age 81. Dr Lee was a 1932 graduate of Columbia University College of Physicians and Surgeons. He was a member of the Medical Society of the County of Oneida and the Medical Society of the State of New York.

George Charles Linn, MD, Highland Beach, Florida. Died November 27, 1985; age 77. Dr Linn was a 1933 graduate of Columbia University College of Physicians and Surgeons. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Robert D. Phelps, DO, Buffalo. Died January 22, 1986; age 60. Dr Phelps was a 1953 graduate of Philadelphia College of Osteopathic Medicine. He was a member of the Medical Society of the County of Erie and the Medical Society of the State of New York.

Anthony Frederick Rizzo, MD, Delray Beach, Florida. Died January 9, 1986; age 73. Dr Rizzo was a 1938 graduate of University of Buffalo School of Medicine. He was a Fellow of the American Academy of Family Practice and a member of the Medical Society of the County of Monroe and the Medical Society of the State of New York.

Hans Selzer, MD, Brooklyn. Died February 16, 1986; age 77. He was a 1933 graduate of Medizinische Fakultät der Universität, Wien. Dr Selzer was a Fellow of the American College of Anesthesiologists and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Richard M. Silberstein, MD, Staten Island. Died February 3, 1986; age 64. He was a 1946 graduate of the University of Pittsburgh School of Medicine. Dr Silberstein was a Diplomate of the American Board of Psychiatry and Neurology and a member of the Academy of Medicine, the American Psychoanalytic Association, the American Psychiatric Association, the American Academy of Child Psychiatry, the American Public Health Association, the Pan American Medical Association, the Richmond County Medical Society, and the Medical Society of the State of New York.

Robert Fogler Solley, MD, Los Osos, California. Died February 17, 1986; age 85. Dr Solley was a 1926 graduate of Columbia University College of Physicians and Surgeons. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Jose R. Sotolongo, MD, Elmhurst. Died November 23, 1985; age 61. Dr Sotolongo was a 1949 graduate of Universidad de la Habana Facultad de Medicina y Farmacia. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Jacob J. Wineburgh, MD, New Hartford. Died February 21, 1986; age 88. Dr Wineburgh was a 1923 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a member of the Medical Society of the County of Oneida and the Medical Society of the State of New York.

Guidelines for authors

Originality

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089-1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

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An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), an abbreviated title of no greater than 40 spaces for use as a running foot, and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

Categories

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

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The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

References

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

References should be indicated in the text by superscript numbers following the name of the author (eg, Smith[2] reported two cases).

The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear on the text. When there are six or fewer authors, all should be listed; where there are seven or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83:925-927.
2. McGuigan JE. Peptic ulcer. In: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD, eds. *Harrison's Principles of Internal Medicine*. New York, McGraw-Hill, 1983, pp 1697-1712.

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All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

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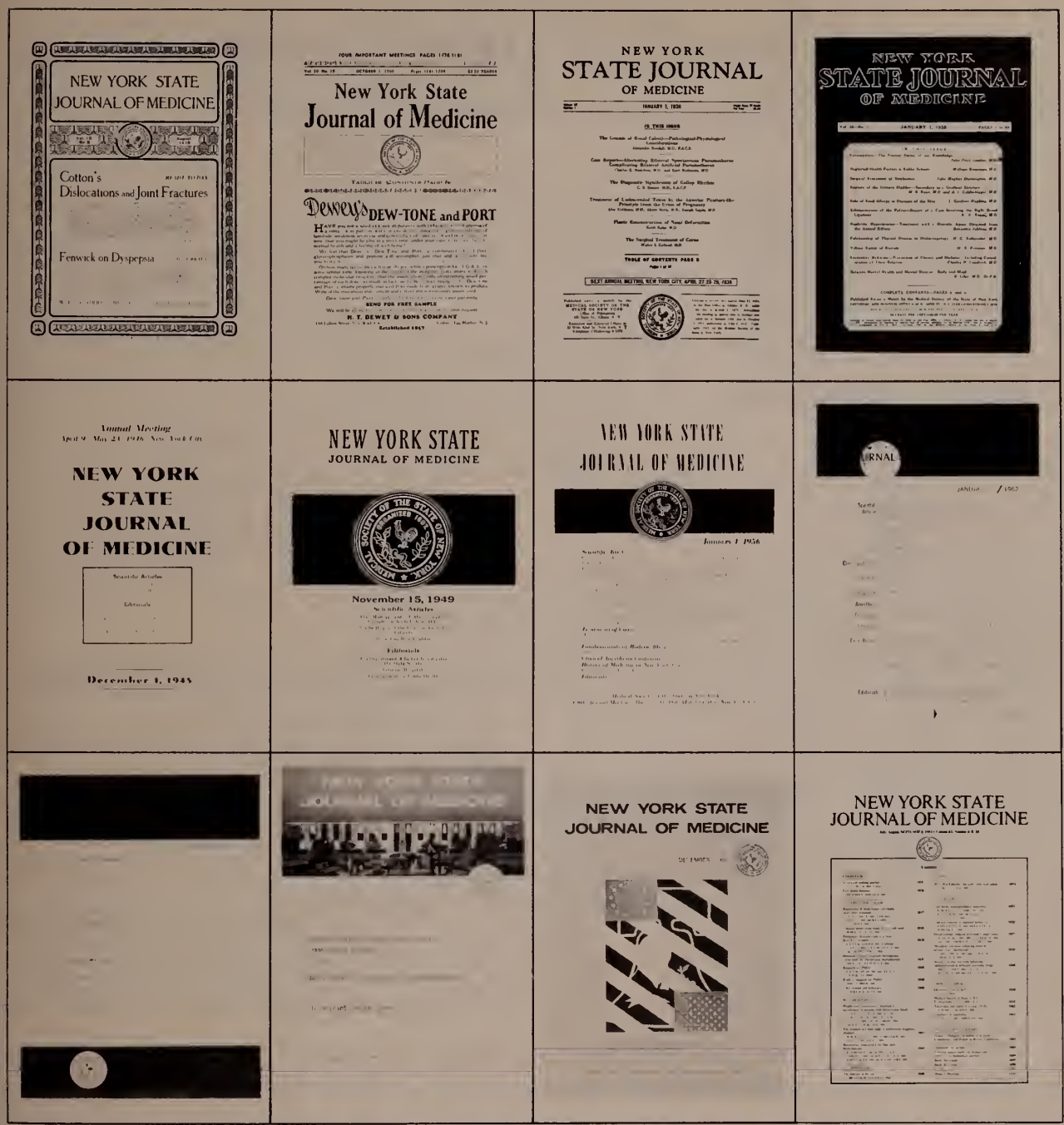

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June 13–14. **Update in Obstetrics and Gynecology.** 10 Cat 1 Credits. Info: University of Kentucky College of Medicine, Office of Continuing Education, 132 COM Building, Lexington, KY 40536-0086. Tel: (606) 233-5161.

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June 13–14. **New Developments in Diagnosis and Pharmacotherapy of Infectious Hypertension and Rheumatic Diseases.** Sheraton Hotel, Portland. Info: American College of Physicians, 4200 Pine St, Philadelphia, PA 19104. Tel: (800) 523-1546.

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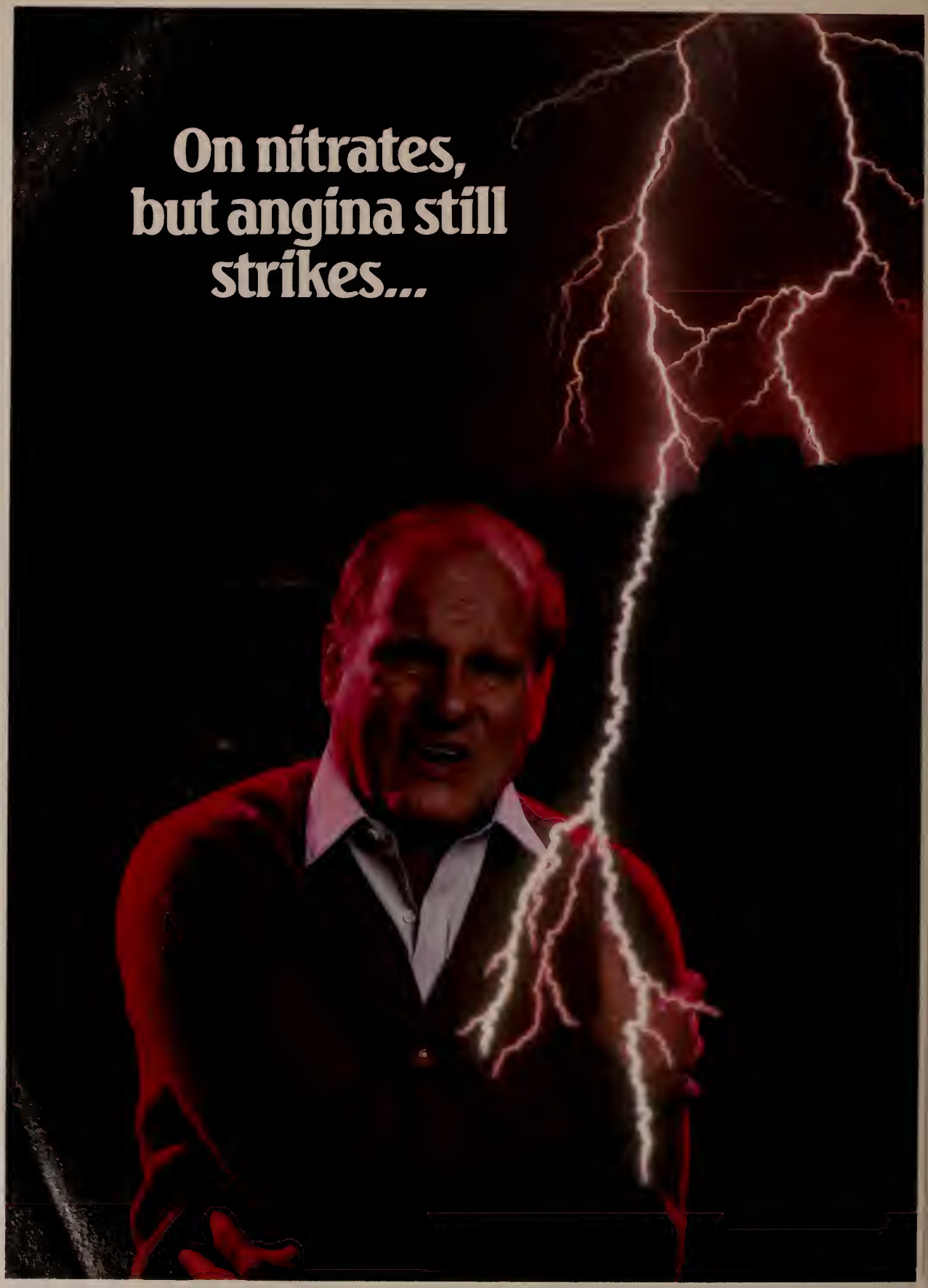
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Marked 1° or progressive 2° or 3° AV block requires a dosage reduction or, rarely, discontinuation and institution of appropriate therapy depending upon the clinical situation. Patients with hypertrophic cardiomyopathy (IHSS) received verapamil in doses up to 720 mg/day. It must be appreciated that this group of patients had a serious disease with a high mortality rate and that most were refractory or intolerant to propranolol. A variety of serious adverse effects were seen in this group of patients including sinus bradycardia, 2° AV block, sinus arrest, pulmonary edema and/or severe hypotension. 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(See *Warnings.*) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecomastia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984 2385

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June 6. **Treatment of Sexually Abused and Traumatized Clients.** Info: The Health and Education Council, Inc, 7201 Rossville Blvd, Baltimore, MD 21237. Tel: (301) 686-3610.

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June 16–18. **Fourth International Workshop on Operative Digestive Endoscopy.** Erasme Hospital, Brussels. Info: Andrea Siroka, NYU Medical Center, Suite 4-F, 530 First Ave, New York, NY 10016. Tel: (212) 340-7245.

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June 6–7. **Toronto Neurology Update.** 13 Cat 1 Credits. Info: Ann McCreath, Organizing Secretary, Sunnybrook Hospital, University of Toronto Clinic, 2075 Bayview Ave, Toronto, Ontario M4N 3M5. Tel: (416) 480-4959.

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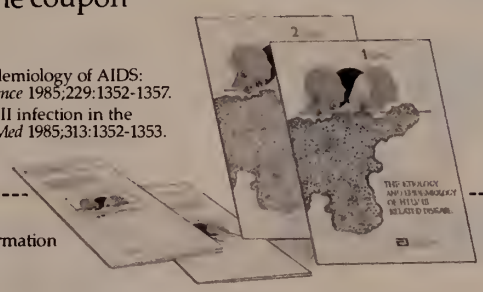

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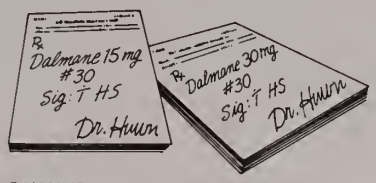

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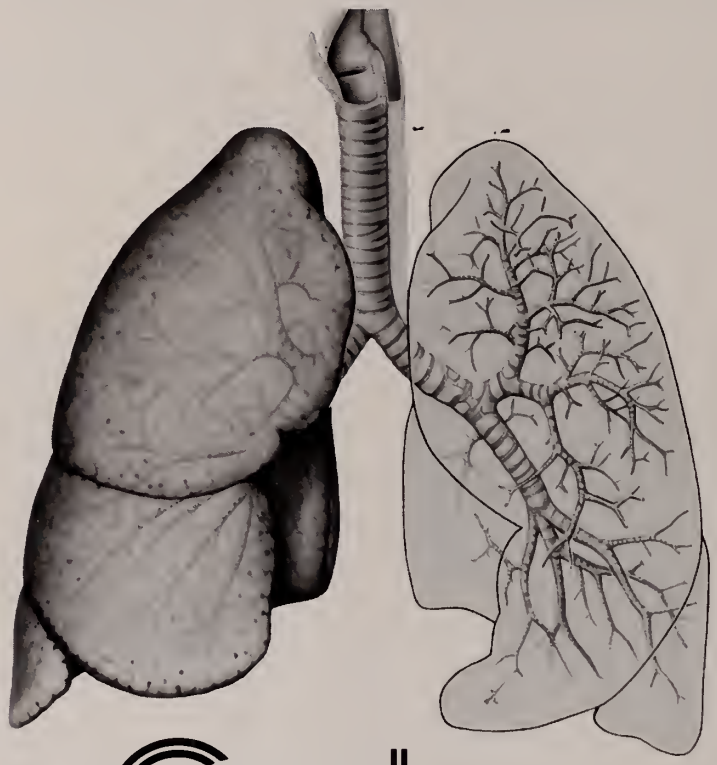

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Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Such elevations may disappear even with continued treatment; however, four cases of hepatocellular injury by verapamil have been proven by rechallenge. Periodic monitoring of liver function is prudent during verapamil therapy. Patients with atrial flutter or fibrillation and an accessory AV pathway (e.g. W-P-W or L-G-L syndromes) may develop increased antegrade conduction across the aberrant pathway bypassing the AV node, producing a very rapid ventricular response after receiving ISOPTIN (or digitalis). Treatment is usually D.C.-cardioversion, which has been used safely and effectively after ISOPTIN. Because of verapamil's effect on AV conduction and the SA node, 1° AV block and transient bradycardia may occur. High grade block, however, has been infrequently observed. 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Chronic ISOPTIN treatment increases serum digoxin levels by 50% to 70% during the first week of therapy, which can result in digitalis toxicity. The digoxin dose should be reduced when ISOPTIN is given, and the patients should be carefully monitored to avoid over- or under-digitalization. ISOPTIN may have an additive effect on lowering blood pressure in patients receiving oral antihypertensive agents. Disopyramide should not be given within 48 hours before or 24 hours after ISOPTIN administration. Until further data are obtained, combined ISOPTIN and quinidine therapy in patients with hypertrophic cardiomyopathy should probably be avoided, since significant hypotension may result. Clinical experience with the concomitant use of ISOPTIN and short- and long-acting nitrates suggest beneficial interaction without undesirable drug interactions. Adequate animal carcinogenicity studies have not been performed. 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(See *Warnings.*) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecomastia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984 2385

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SUFFOLK

July 28-Aug 1. **Current Issues in Mental Health. Borderline and Other Personality Disorders: Diagnosis, Integrated Treatment, and Pharmacotherapy.** Southampton. Info: Ms Jane Smyth, Administrator, Hampton Summer Institute, 128 East 56th St, Box 430, New York, NY 10022. Tel: (718) 268-4952.

ERIE

July 14–17. **10th International Convocation of Immunology.** Info: Dr James F. Mohn, Director, The Ernest Witebsky Center for Immunology, 210 Sherman Hall, State University of New York at Buffalo, Buffalo, NY 14214. Tel: (716) 831-2848.

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CALIFORNIA

July 21–25. **Internal Medicine: 34th Annual Update and Board Review.** 40 Cat 1 Credits. Los Angeles. Info: American College of Physicians, P.O. Box 7777-R-0510, Philadelphia, PA 19175. Tel: (800) 523-1546.

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CENTER OR CLINIC

- Central facility or facilities
- Staff physicians
- Patient selects a primary care physician (Internist, GP, FP, and Pediatrician) from the staff
- May frequently have physician turnover resulting in short term doctor-patient relationship and/or the need to re-select primary physician

DIRECT PHYSICIAN CONTRACTING

- No central facility
- Private practicing physicians
- Patient selects a primary care physician (Internist, GP, FP, Pediatrician)
- Obstetrician-Gynecologist is not a primary, but a specialist. The patient is seen by the Obstetrician-Gynecologist only by referral from the primary care physician.
- Primary physicians are capitated. That means they are paid a fixed amount annually to treat a specific patient whether they see that patient once—or a hundred times.
- No group voice because there is no physician group
- Specialists are reimbursed a percentage of their fee
- Patients can see physicians when they want

IPA CORPORATIONS

- No central facility
- Private practicing physicians
- Patient selects 1 or 2 primary physicians: Female and male adults select an Internist, GP or FP; females additionally select an Obstetrician-Gynecologist; parents select a Pediatrician, GP or FP for their child(ren).

  Obstetrician-gynecologists are primary care physicians, and can be seen directly by the member for both routine and specialized care with no referral necessary.
- A corporate body which is organized by physicians. The IPA then contracts with an HMO to provide services to the HMO members. *The physician does not join the HMO, but simply participates.*
- The IPA is the physicians' voice to the HMO which represents the physician re: fee reimbursement, quality of care, peer review, etc.
- Traditional fee-for-service payment
- Patients can see physicians when needed. Each visit is paid for by the HMO on a fee-for-service basis

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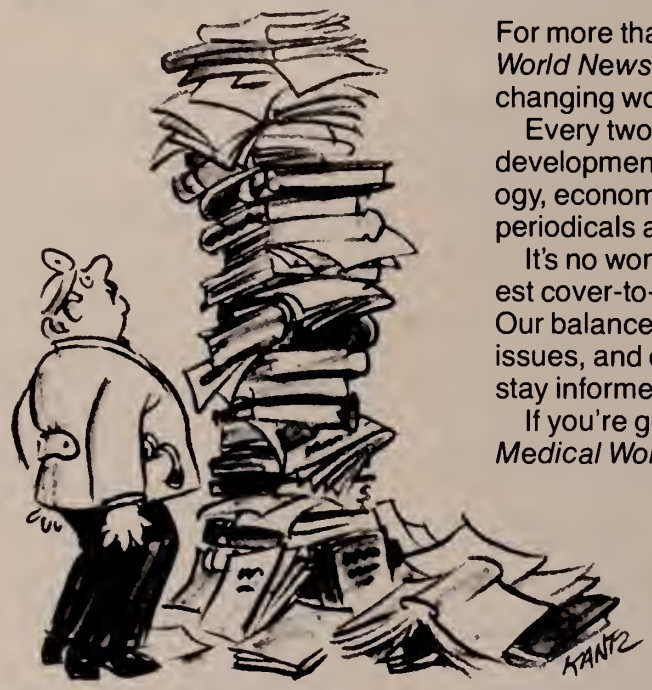

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- ***Proven efficacy when used alone in angina***[1,4-6]
- ***Compatible with both beta-blockers and nitrates***[7]

Please see brief summary of prescribing information on the next page.

CARDIZEM® 60 mg tid or qid

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FEWER SIDE EFFECTS IN ANTIANGINAL THERAPY

BRIEF SUMMARY

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist).

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM (diltiazem hydrochloride) in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGDT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other	Polyuria, nocturia.

The following additional experiences have been noted.

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGDT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** — CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

CARDIZEM 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other. Issued 4/1/84

See complete Professional Use Information before prescribing.

0642T5

References: **1.** *Physicians' Desk Reference®*, ed 39. Oradell, NJ, Medical Economics Company Inc, 1985. **2.** Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): *Heart Disease. A Textbook of Cardiovascular Medicine*, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. **3.** Schroeder JS: Calcium and beta blockers in ischemic heart disease. When to use which. *Mod Med* 1982; 50(Sept):94-116. **4.** Subramanian VB: Comparative evaluation of four calcium antagonists and propranolol with placebo in patients with chronic stable angina. *Cardiovasc Rev Rep* 1984; 5:91-104. **5.** Schroeder JS, Feldman RL, Giles TD, et al: Multiclinic controlled trial of diltiazem for Prinzmetal's angina. *Am J Med* 1982; 72:227-231. **6.** Weiner DA, McCabe CH, Cutler SS, et al: The efficacy and safety of high-dose verapamil and diltiazem in the long-term treatment of stable exertional angina. *Clin Cardiol* 1985; 7:648-653. **7.** Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. *Consultant* 1984; 24(Dec):150-159.

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JOURNAL OF MEDICINE

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COMMENTARIES

Controlling cervical cancer

The latest statistics from the American Cancer Society reaffirm the decline in the incidence and mortality from invasive cancer of the cervix.[1] As the rising incidence of lung cancer associated with smoking in women and the intractable mortality from breast cancer dominate our consciousness, we often forget that the low rates of invasive cervical cancer are sustained only by constant vigilance. New York State still reports 1,200 new cases of invasive cervical cancer and 460 cervical cancer deaths each year.[2] More than 60% of other cancer deaths in women living in New York State occur over the age of 65. However, almost two thirds of New York State women who die from cervical cancer are under age 65. One third of those who die are younger than 55 years, economically productive, and frequently the mothers of dependent children. Howe and Bzduch's report in this issue of the *Journal*[3] is timely because it pinpoints both the successes and the limits of Pap smear screening, and identifies areas where further efforts may make a difference.

Howe and Bzduch report that 97% of women living in upstate New York had at least one Pap smear in their lifetime; 82% had a smear within three years and 60% had one within a year. Their results are consistent with Hendershot's report using national data in which 92% of women 25 to 44 years of age had been screened within three years.[4] The results are also consistent with other local data such as Celentano's Maryland survey in which 79% of women under age 65 had been screened in the previous two years.[5] Also encouraging in Howe and Bzduch's report is that women with high risk factors such as early intercourse and multiple sexual partners were more likely to have been screened than women without these risk factors. But the high screening levels reported by Howe and Bzduch are probably maximal, because minority women and women with limited education were under-represented in the survey. Yet minority and poorly-educated women are at above-average risk for developing cervical neoplasia. Indeed Howe and Bzduch's survey found that women with limited education—a surrogate for poverty[6]—were less likely to have been screened than more educated women, a difference independent of age. Therefore, Howe and Bzduch are justifiably concerned with how the Pap smear screening level may be improved.

Effective screening for the total population at risk for cervical cancer requires many levels of activity: (1) Maintaining a high level of screening among younger women through fertility-related health services; (2) Expanding the level of preventive gynecologic care in non-fertile premenopausal and postmenopausal women; and (3) Identifying groups of women at above-average risk for cervical neoplasia and groups of women with below-average screening levels, and focussing education and intervention on these groups.

The high level of screening in younger women in New York State has been achieved by the inclusion of Pap smears as a routine part of all obstetric and gynecologic care. The introduction of the Pap smear on a large scale coincided with the expansion of medically-prescribed contraception in the 1960s and 1970s and with the introduction of legal abortion in 1970. Since sexual activity itself is a risk factor for cervical neoplasia, the provision of the Pap smear in fertility-related services guaranteed that a large proportion of the women at risk would be screened. Such large-scale implementation of screening was particularly critical because concurrent changes in sexual activity in young women (including intercourse at younger ages and more sexual partners) may well have increased the risk of cervical neoplasia. Starreveld and associates, for example, documented a rising incidence of carcinoma in situ of the cervix in young women in Alberta since 1973.[7] This may well be paralleled in New York State.

The complex changes in sexual behavior, contraception,

desired family size, and women's employment during the past 25 years have led to higher levels of fertility control. These higher levels are increasingly achieved by sterilization. In 1982, 41% of all US women aged 15 to 44 and 63% of women aged 35 to 44 depended on sterilization for contraception.[8] Consequently a large proportion of women who would previously have sought medical care for contraception or pregnancy no longer need such services. However, these women are at the ages where the incidence of carcinoma in situ of the cervix and invasive cancer of the cervix increases rapidly. Women at greatest risk for cervical cancer—low income women who had early coitus, pregnancies in their teens, and reached their desired family size early—are among those likely to choose sterilization in their late 20s or early 30s. A 1976 report showed that women who had been sterilized were less likely to have had a recent Pap smear than women who used other forms of contraception.[9]

Women who have been sterilized, like post-menopausal women,[5] are probably more likely to use general practitioners or internists, rather than gynecologists, as their primary care physicians. Therefore the responsibility for providing preventive care for genital and breast cancer or for referring women for such care will fall increasingly on non-gynecologists.

Howe and Bzduch demonstrate that women over 45 comprise the largest group who had contacts with the medical system but were not screened (what they term the "potential missed opportunity" group). This finding is consistent with other reports that many older women with invasive cervical cancer who received previous medical or hospital care had not received a Pap smear.[10]

Clearly a critical factor in the continued control of cervical cancer is ensuring gynecologic care for nonfertile women, both post-menopausal women and the increasing group of women who are voluntarily infertile. Such care may have the additional benefit of enhancing the early detection of other genital cancers and perhaps even breast cancer as well. Although no simple, inexpensive screening test for endometrial cancer exists, regular gynecologic care may play a role in the early detection of this most common of gynecologic malignancies. A combination of cytology examination, pelvic examination, and immediate investigation of symptoms may contribute to the early detection of endometrial cancer. The above-average stage at diagnosis and high mortality from endometrial cancer in minority and low-income women suggest that social-behavorial factors may play a significant role in limiting early detection. Lack of gynecologic care may be one critical factor.

In this context, the controversy that followed the American Cancer Society's 1980 recommendations for screening every three years[11] was modified in a National Institutes of Health (NIH) consensus to screening every one to three years at the physician's and woman's discretion.[12] In Canada as well, the original recommendation of the 1976 Walton report for triennial screening has been modified to screening every year to the age of 35 years, followed by screening every five years.[13] The American Cancer Society has recommended annual pelvic examinations after the age of 45 years as the standard of care for older women. Such standards are yet to be achieved.

Sustained screening in fertility-related services and expanded screening for infertile and postmenopausal women would ensure routine Pap smear screening for women of all ages. It is also essential to identify women at unusual risk for cervical neoplasia or women who have not been screened. Immunosuppressed women are at above-average risk for cervical neoplasia; such women include patients having received organ transplants, those with autoimmune diseases receiving immunosuppressive medication, and genetically immunodeficient women.[14] Women who have not been screened include immigrants from countries with limited health services. Of particular concern are immigrants from Latin American and Caribbean countries which have high incidences of cervical cancer.[15] Although specific media campaigns, focused health education sessions, and screening programs can raise the level of awareness among these special groups of women at risk, the primary physician who treats the immunosuppressed woman, the immigrant woman, or any other woman at risk is probably the most important person to influence whether the patient seeks out and receives preventive care, such as a Pap smear.

The "missed opportunities" that Howe and Bzduch describe are opportunities missed by the medical care system and as such are of primary concern to the readers of this journal. However, clearly the women themselves may also have missed many opportunities to request screening or referral as part of their care. For the 20% of the survey population who had no contact with the medical system (the "no opportunity" group), screening levels may only be improved by increasing awareness among women of the efficacy of Pap smears and the necessity of making preventive care a priority.

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The Mallory-Weiss and Boerhaave syndromes

The examples reported in this issue of the *Journal* of lower esophageal injuries due to forceful and uncontrolled vomiting are worthy of study and reflection by those in the medical profession. Early reports of Mallory-Weiss tears and the Boerhaave syndrome tended to associate these occurrences solely with alcoholic binges and commonly among destitute individuals. It is now known that these entities also occur among the respectable members of society, both as part of another illness and as a primary event. As properly pointed out by Pezzulli and associates,[1] the Mallory-Weiss syndrome, which was once thought to be rare, is now commonly seen. It would not be surprising if many of the so-called blind gastric resections in the past for upper gastrointestinal bleeding where bleeding had momentarily stopped at the time of exploration were indeed for this entity.

The development of flexible endoscopes has immeasurably facilitated the diagnosis and treatment of gastrointestinal bleeding, particularly in this specific group of patients where there is a higher incidence of cirrhosis and consequent suspicion of portal hypertension as a causative agent in the hemorrhage. Although often successful, endoscopic diagnosis may be problematic, particularly in the presence of massive bleeding where the viewing medium cannot be cleared enough for accurate identification of the bleeding source. In these instances, radionuclide bleeding scans and selective arterial studies are essential; the old fashioned barium meal may also on occasion provide the necessary information.

Almost all cases of upper gastrointestinal bleeding are initially treated conservatively, as indicated by Pezzulli and colleagues. Most patients with the Mallory-Weiss syndrome stop bleeding with gastric decompression, sedation, and acid control intravenously and by instillation with lavage. The few patients who fail a conservative trial need the most accurate diagnosis possible relating to location and etiology of the bleeding. A plan should then be formulated depending on what is found. Expert endoscopists claim that on occasion a single bleeding point may be seen in a Mallory-Weiss tear that can be treated by fulguration. As with all other methods of treatment there is risk; the risk involved with this maneuver is perforation. If a selective arteriogram is done to locate the bleeding, a plan for vasopressin infusion should be on hand, or if and when the expertise of the interventionist radiologist allows for embolization.[2] All of these methods have their own peculiar risks and complications and success is, to a large extent, dependent on the individual who carries them out. The left gastric artery ordinarily allows embolization unless the stomach has earlier been deprived of some of its blood supply.

There are times when the necessary ancillary facilities are not available and when laparotomy and plication of the mucosal tear becomes necessary. At that time the surgeon has to determine how accurate the diagnosis is, and whether other factors such as acid peptic disease play a role in the bleeding, making a more extensive procedure necessary.

The Boerhaave syndrome is much more of a management problem than the Mallory-Weiss tear, and understandably so since it involves the rupture of the organ with intestinal contents spilling into the mediastinum and often into the free pleural cavity. Surgeons are frequently confronted with esophageal perforations, mostly iatrogenic ones from dilatations, endoscopy, and biopsy procedures. Most of these occur in the hospital and are anticipated, so that immediate remedy may be offered. In spite of the injury happening under the physician's eye, it may be difficult to determine the appropriate treatment. The common cervical esophageal perforation occurring during rigid endoscopy is ordinarily treated by simple synaclavicular drainage. Esophageal rupture caused by balloon dilatation, most similar to the Boerhaave syndrome, is usually treated by thoracotomy, drainage, closure of the perforation, gastrostomy, and feeding jejunostomy.

In spite of the occurrence of perforation during therapeutic maneuvers, it is often not clear how much damage has been done and how much treatment is necessary. Incomplete tears without air in the mediastinum or pleural effusions often heal with conservative treatment. Conversely, it is important to recognize complete rupture since immediate repair offers the best result. Contrast examination of the esophagus offers the best evidence of the magnitude of the injury and should be undertaken with a water soluble medium as soon as a suspicion of esophageal injury is present.

The patient with the Boerhaave syndrome is rarely seen immediately following injury. Due to social circumstances, complaints are often missed or misinterpreted and the chance of immediate repair is lost. There are certain pieces of information that aid in the evaluation of these patients. Among these are the history surrounding the illness; chest pain, pleural effusion, air in the mediastinum, and pneumothorax on chest films and then confirmation by contrast study. The treatment described by Canver in this issue of the *Journal* is exemplary, once the

diagnosis was made.[3] It is rare to have complete success by closed chest drainage alone. The esophagus, however, has remarkable healing qualities and with complete esophageal exclusion, gastrostomy, and a feeding jejunostomy, success may be achieved if a loculated hydropneumothorax has not occurred and if the lung expands after closed drainage. Many surgeons are loath to resort early on to complete esophageal diversion, since on occasion the perforation in the esophagus does not heal. The surviving patient is then left with a draining chest wound. A colon interposition is the remaining choice for re-establishing gastrointestinal continuity.

The formidable overall mortality from the Boerhaave syndrome, however, warrants truly heroic measures in order to salvage the patient. In those instances where diagnosis is delayed, a complete cervical esophageal diversion with gastrostomy and feeding jejunostomy are in order. Some surgeons have resorted to exclusion of the abdominal esophagus to avoid regurgitation from the stomach, but ordinarily a good gastrostomy should suffice. Treatment of the local perforation has to be individualized. Early perforations warrant primary repair through thoracotomy. Occasionally these may be reinforced using a Nissen fundus wrap around the repaired area.[4] If a good repair is obtained, esophageal diversion may be avoided but gastrostomy and a feeding jejunostomy are still necessary.

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Hepatic rupture and pregnancy

The report on spontaneous liver rupture in pregnancy by Heller and Goldfarb in this issue of the *Journal* reminds us of the serious morbidity associated with this unusual complication of pregnancy. The patient described underwent three major operations and two minor procedures. She received 14 units of packed red blood cells, 8 units of fresh frozen plasma, and 25 units of platelets. She was hospitalized for 32 days, but unlike many patients with liver rupture this patient survived.[1]

In 1976, Bis and Waxman[2] published an extensive review summarizing the literature on 91 cases of liver rupture associated with pregnancy. Using this review as a background, I would like to comment on the changes that have occurred during the past decade with respect to the management of patients with suspected or confirmed liver rupture during pregnancy and the early puerperium. The multidisciplinary approach to the care of these patients is intended to be a primary point of this commentary.

In the cases reported up until the mid 1970s, maternal mortality was 59% and fetal mortality was 62%. Preoperative diagnosis was correct in less than 10% of cases, and laboratory means for diagnosis most often included only a complete blood count and vague radiographic evidence of intraabdominal hemorrhage. The authors did note that liver scans had been successfully used to diagnose liver rupture.

In the review by Bis and Waxman, the need for prompt surgery was stressed to the point that it was stated "No patient survives without surgery. . .The only hope of survival is surgical intervention."[2] Treatment methods included digital compression, packing with a variety of materials, suturing, electrocoagulation, and topical application of adhesives or plastics.

New diagnostic tests have become available during the ten years that have elapsed since the publication of this comprehensive report. The need for surgery in all cases has been challenged, additional techniques to achieve hemostasis have been developed, the intensive care of the critically ill patient has become refined, and more attention has been directed toward liver abnormalities in pregnant patients with hypertension. Collectively, these changes highlight the need for a prompt, multidisciplinary approach in patients with suspected or diagnosed liver rupture if maternal and fetal outcome is to be maximized.

The ability to diagnose liver rupture has improved significantly. Ultrasound, computed tomography, and radionuclide scans have all been used successfully,[3-5] and the ease and safety with which these scanning procedures may be performed make such evaluation practical in those patients who are either pregnant or recently delivered who complain of significant right upper quadrant pain. Selective angiography has also been useful in detecting liver

rupture.[6]

The number of methods to achieve hemostasis in patients with liver rupture has also increased during the past few years.[7,8] In addition to suturing, packing, and digital compression, cessation of blood flow by either direct vascular ligation[9] or by arterial embolization of Gelfoam or other material may be achieved.[10] The number of topical agents for achieving hemostasis has also increased with topical thrombin, microfibrillar collagen, and regenerated cellulose now available.[7] Since many cases of liver rupture are detected intraoperatively, as the case presented in this issue illustrates, the need for techniques to achieve hemostasis is acute, and the more options available, the better.

Probably the most significant change concerning liver rupture in pregnancy involves the need for surgical intervention. Until recently, a number of reports (including ours in 1982[7]) continued to stress the need for prompt celiotomy once hepatic rupture was identified. However, successful outcome has also been reported with conservative management. In three reports,[5,11,12] ten patients recovered without surgical treatment of the liver. Of these ten patients, the diagnosis of hepatic rupture was made prior to delivery in six, all of whom underwent cesarean delivery. In the other four patients, diagnosis was made within 48 hours following vaginal delivery. All of the patients recovered; subsequent serial scans indicated diminution in size of the hematomas.

Since many patients with liver rupture require a level of care not available at smaller hospitals, transfer to more thoroughly equipped facilities is often desirable. Packing of the liver rupture site with gauze[7,13] and use of the gravity suit[14] are techniques that may make such a transfer more successful. The gravity suit (G-suit) is a double-layered, polyvinyl device that when inflated with air to 10 to 40 mm Hg, provides external counter-pressure to the abdomen and lower extremities. The suit can cause an increase in blood pressure and a decrease in intraabdominal bleeding, most likely by increasing peripheral resistance. Hibbard[15] reported use of the gravity suit in the only two of eight patients with liver rupture who survived. As experience with the gravity suit has increased in nonpregnant patients with intraabdominal bleeding, it is a worthwhile option to consider in patients with liver rupture.

Improved intensive care for all critically ill patients, including those with hepatic rupture, contributes to a better prognosis. Improved blood banking procedures have made massive transfusions possible, thereby allowing multiple surgical attempts to insure hemostasis. There is no doubt that attention to coagulation abnormalities, refined blood typing, and avoidance of transfusion-related infections, in addition to the many other aspects of intensive care, has played a major role in improved survival.

More attention has been focused on the liver in preeclamptic patients, particularly following the reports of Killam and associates[16] and Weinstein,[17] who separately described marked hepatic changes in certain preeclamptic patients. Although liver abnormalities have been known to exist for many years in patients with preeclampsia, recognition of a certain subset of these patients with hemolysis (H), elevated liver enzymes (EL), and low platelets (LP)—the so called HELLP syndrome—has made routine testing of these parameters more common in such patients. Although no direct association has been reported between patients with the HELLP syndrome and those with liver rupture, the fact that this organ is receiving more and more attention in hypertensive patients should prompt earlier evaluation for possible liver rupture.

To summarize, those patients who are pregnant or recently delivered, especially those who are hypertensive, should be evaluated for liver rupture if they complain of significant right upper quadrant pain. Ultrasound and computed tomography scans, if available, are capable of detecting significant ruptures. Selective angiography is another important technique. Once a subcapsular hematoma is identified, expectant management should be considered if the patient is hematologically stable. However, preparations must be made for surgery and constant vigilance for rapid deterioration is critical. If an unruptured subcapsular hematoma is noted during a cesarean delivery, an expectant approach with careful surveillance is most likely warranted if the patient is stable. However, any patient with vigorous bleeding from the liver, detected preoperatively or intraoperatively, should undergo prompt celiotomy to stop the bleeding.

The traditional suturing, compression, and application of topical agents should be attempted initially, with more extensive vascular surgery or partial lobectomy reserved for patients with persistent bleeding. If hemorrhage is noted preoperatively, and personnel skilled in arterial embolization are available, this procedure may make celiotomy unnecessary. If bleeding is uncontrollable, packing with gauze or the use of the gravity suit may be helpful, especially to enable transfer to a tertiary level care center.

The improvements made over the past decade in the diagnosis and treatment of patients with hepatic rupture are indeed encouraging, but this rare complication of pregnancy remains among the most serious ever seen in obstetrics. Physicians from many medical disciplines, including obstetrician/gynecologists, anesthesiologists, radiologists, internists, and others, must be closely involved with these patients if outcome for both mother and infant is to be optimal.

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Should the Medical Society of the State of New York form a union?

The traditional role of the physician as a legal "independent contractor" has been eroded by the evolution of full-time paid hospital staff, implementation of prospective payment systems, cost restraint measures, an attempt by government to control physicians' practices through the hospital, development of PPOs and HMOs, and even the alliances of independent hospitals in specific geographic areas. Consequently, physicians are attempting to find ways out of what they perceive as a threatening situation.

The developing question of separate incorporation of medical staff has raised the issue of the possible unionization of physicians and the concerted action that would flow as a result of such a decision. Hospitals obviously view this concept with considerable concern. If the hospital had to bargain with its medical staff, the "gatekeepers" of its very existence, it would surely be in a disadvantaged position. However, most attorneys agree that hospitals have no obligation under the National Labor Relations Act to recognize a labor union for physicians because physicians are considered independent contractors and are not common law employees of the hospital.

Nevertheless, the pressures on physicians are mounting. A classic economic case of rising supply and declining demand is facing today's physicians. They are further encroached upon in their practice patterns, being second-guessed and told what level of care and length of stay is appropriate for their patients.

As a result of these fundamental changes in the perception of their profession and socioeconomic erosion of their status, physicians are looking for a deliverance and relief from the pressure. It seems that the younger the physician, the greater the anxiety. The older practitioner frequently has established financial stability. The younger physician has leftover debts, unfilled appointment books, and soaring overhead costs, including rapidly escalating malpractice insurance premiums.

Faced with what they perceive to be a steady erosion of professional autonomy and control over the practice of medicine, it is not surprising that physicians are beginning to seriously consider collective action. Although most physicians still regard a physician's union as a contradiction in terms, a growing number of physicians (an estimated 25,000 nationally) are already participating in unions. This is a relatively small number, but I believe it is a measure of the drastic change taking place in the delivery of health care, especially in a profession that has prided itself on individualism.

Massachusetts recently became the eighth state in the nation and the first in the East to establish a physicians' union. Its organizers (not the state medical association) cite several new factors in the medical climate—for-profit medicine, intensified efforts to reduce hospital use, and the physician glut—that now make unionization feasible. According to Dr John LaRossa, president of the newly organized Physicians and Surgeons Association of Massachusetts, the most important contributing factor to unionization (collective action) is the absolute loss of control physicians are experiencing in treating their patients.

According to its founder, the new Massachusetts union will represent physicians in two basic ways. It will bargain collectively on behalf of the growing number of physicians who are salaried employees of hospitals, HMOs, or surgery centers, and it will also represent private practicing physicians as they negotiate individually with third-party payers, including Medicare and Medicaid.

A closer review of the newly formed Physicians and Surgeons Association of Massachusetts (PSAM) reveals the following specific goals:

- Representation of employed (salaried) physicians in collective bargaining over wages and working conditions.
- Operation of an insurance grievance office to represent physicians (individuals) in claim disputes with insurance companies and government agencies.
- Representation of private practicing physicians in individual contract negotiations or renegotiations with third-party payers, hospitals, government agencies and HMOs in order to ensure due process for physicians whose privileges have been unjustly reduced or denied by the hospital.
- Lobbying on matters of concern to physicians and patients.
- Dealing with the business community in those instances where the union believes physicians' or patients' rights are being abrogated by business interests.

The question then is whether the Medical Society of the State of New York (MSSNY) should form a union or create a separate entity for that purpose to insulate itself from possible antitrust charges. Of course, any organization or group can unionize. The key is that if its members are not traditional employees, the union engages in activities at its own peril without the protection of the National Labor Relations Act. Thus, any collective action taken by physicians who do not meet the test of being traditional employees would make them subject to antitrust actions. This doctrine would appear to apply to a union formed by MSSNY or one formed as part of a separate but related corporation. Moreover, as we studied the union concept, we discovered that most of the activities being attributed to a physician union could be conducted by MSSNY. One further thought on the need for a physician union is the fact that there are presently too few salaried physicians in any one locale in New York to have sufficient influence to warrant collective action.

Much of the frustration of physicians such as those in Massachusetts stems from a perception that the state medical association has been unsuccessful as the physicians' advocate and that, therefore, a new organization is needed to represent their interests. Therefore, it would seem that if MSSNY could take a more aggressive posture on behalf of its individual members, we could preclude any reason to form a separate union organization for so-called collective bargaining purposes while at the same time strengthening the viability of MSSNY. It is interesting to note that MSSNY could and has been performing to a limited degree, all of the above-mentioned activities embraced by PSAM with the exception of the first item (collective bargaining). We have already indicated that at the present time, there are probably too few salaried physicians who are considered legitimate employees concentrated in one locale who could benefit from collective bargaining.

Thus, it would appear logical that MSSNY create a special in-house Physician Support Service activity that would perform the functions listed above. Additionally, our Physician Support Services activity could also coordinate, through broker arrangements with credible outside experts, the provision of negotiating services, financial services, investment services, and practice management services.

In my judgment, one of the most important services that such an activity could perform would be to assist physicians in resolving reimbursement problems with third-party carriers.

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of New York

Adapted from *Indiana Medicine* 1986; 79:45–46.

George J. Lawrence, Jr, MD

George J. Lawrence, Jr, MD, retires this month as Executive Vice-President of the Medical Society of the State of New York (MSSNY), a position in which he has served with great distinction since March 4, 1985. Dr Lawrence received his MD degree from the University of Pennsylvania in 1938 and interned at Kings County Hospital. He was born at Flushing Hospital in Queens where his father, George J. Lawrence, Sr, MD, was chief of the Department of Obstetrics and Gynecology. His grandfather, Enoch Pinte Lawrence, MD, was a member of the original medical staff of Flushing Hospital in 1884.

Dr Lawrence is a Diplomate of the American Board of Obstetrics and Gynecology and a Fellow of both the American College of Obstetricians and Gynecologists and of the American College of Surgery. He practiced obstetrics and gynecology for 34 years and served as director of the Department of Obstetrics and Gynecology at Flushing Hospital and Medical Center. He is currently director emeritus and attending emeritus in Obstetrics and Gynecology at Flushing Hospital.

In 1974 Dr Lawrence became Director of the Division of Scientific Activities at MSSNY, in which position he greatly advanced the Society's Continuing Medical Education program. A member of MSSNY since 1940, he was a delegate to the American Medical Association from 1962 to 1968 and a MSSNY councilor for seven years. He served as president of the Medical Society of the County of Queens and is currently chairman emeritus of the Board of Trustees of that society. Dr Lawrence served as a Queens delegate to the MSSNY House of Delegates for 23 years.

"George's contribution to and leadership in organized medicine has been of such high quality as to be immeasurable. I am most gratified that he will continue to be involved in the Society in a consultative capacity."

RALPH SCHWARTZ, MD
Chairman
Board of Trustees
Medical Society of the State of New York

"George J. Lawrence, Jr, has been a member of the Medical Society since 1940 and for over 40 years and has been active as a spokesman and leader for the organized medical profession at the national, state, and county levels. He is a compassionate physician and an accomplished leader."

JOHN FINKBEINER, MD
President
Medical Society of the State of New York

"We all know George's dedication and devotion to medicine, but the courage of his convictions and his intellectual honesty are unsurpassable."

DANIEL F. O'KEEFFE, MD
Past-President
Medical Society of the State of New York

"As a third generation physician, George Lawrence, Jr, MD, and his family have given much of themselves to help ensure the health and well being of generations of New York families. George's love for his profession has been exemplified in his service to organized medicine as president and chairman of the board of the Medical Society of the County of Queens, director of Scientific Activities, and executive vice president of the Medical Society of the State of New York, and as an original member of the AMPAC Board of Trustees."

JAMES H. SAMMONS, MD
Executive Vice President
American Medical Association

A survey of Pap smear screening in upstate New York

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ABSTRACT. A survey of upstate New York female residents, aged 25 to 74, was begun in August 1984 to examine more closely why women have not received uterine cytological examinations in the previous year. The aim of the study was to describe three groups of women who were categorized by Pap smear screening status and medical utilization: women with Pap smears; women who had no medical contacts, and therefore no Pap smears; and women with medical contacts but without Pap smear screening. The survey was completed by 72% of the sample. Of the population studied 19% had been to a physician but had not received a Pap smear and 21% of the women had not seen a physician. The remaining 60% of the women had a Pap smear taken in the last year. Screening status did not differ by race. However, separated and divorced women, women with 13 or more years of education, and women aged 25 to 34 were most likely to have had uterine cytological examinations in the last year. Furthermore, significant differences among the three Pap smear groups were detected by marital status, age, and education. Behavioral risk factors also differed among the three groups but in the direction that the highest risk women were more likely to have had a Pap smear.

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The prevention of advanced-stage disease and death is a primary goal of cancer screening. Strong recommendations for widespread cervical cancer cytological screening were first encouraged by the American Cancer Society in the early 1940s. Widespread adoption of this screening modality occurred by the 1950s. Although the efficacy of the Pap smear was never conclusively determined through randomized clinical trials, voluminous evidence supports it as an effective early detection technique.[1-8]

It is disconcerting that after more than 30 years of screening, cases of invasive cervical cancer and deaths from cervical cancer are still reported in sizable numbers each year to the New York State Cancer Registry. In upstate New York alone (New York State excluding New York City), approximately 600 new cases of invasive cervical cancer and 250 deaths are reported each year.

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The ultimate evaluation of a successful cervical cancer prevention effort is the eradication of cases and deaths from invasive disease. The National Cancer Institute's primary goal is to reduce by half the number of cancer deaths by the year 2000.

Cancer of the cervix is one site that has an easily applied and highly accurate screening tool, the Papanicolaou smear. Detection of malignancies in very early stages is possible and, unlike some cancer detection modalities, with relatively little inconvenience to the patient. Furthermore, malignancies are highly curable when detected in their early stages. Early detection is often feasible with the Papanicolaou smear.

The question this raises is, given the widespread availability and relative simplicity of the method, why do 250 theoretically preventable deaths occur each year in upstate New York alone? More specifically, to what degree may this question be answered by attributing lack of screening to women not presenting themselves for medical care or to physicians not providing the service to all of their female patients?

METHODS

A list for sampling of women, aged 25 to 74, was obtained from the motor vehicle license records of the New York State Department of Motor Vehicles. The women in the sample resided in upstate New York (exclusive of New York City) and they had renewed their driver's license within the previous year. The sample listing included the women's names, addresses, and birthdates.

In May 1984, a systematic sample beginning with a random start was drawn from the computerized listing of records. The selection process was executed by taking every *N*th female who met our criteria until the entire alphabetical listing of licensed drivers had been exhausted. A sample of 1,600 was desired; 1,677 were selected. A questionnaire was mailed to each woman in August 1984, with a cover letter explaining the objectives of the survey and with a stamped return envelope. Follow-up procedures by mail were used to maximize the survey response.

Data from the 1980 US Census were used to determine if the age and residential characteristics of the respondents were similar to those of upstate New York. Geographic location of residence was divided into five regions: (1) Long Island, (2) the rest of Southeastern New York, (3) Northeastern New York, (4) Central New York, and (5) Western New York. Possible biases due to response and coverage of the sampling frame were also evaluated.

The survey instrument included a number of questions on medical service utilization. Among them was the question,

"Have you had a Pap smear in the last year?" In addition, respondents were asked, "Have you seen a physician for any reason in the last year?" If a positive response was given, they were then asked to list each visit with the following information: the reason for the visit, whether the physician did Pap smears, whether they were physically able to have a Pap smear, whether it was an appropriate opportunity for a Pap smear, and whether or not they had a Pap smear during the visit.

The respondents were asked to provide information on several of the risk factors for cervical cancer. They were asked their age at first pregnancy and at first sexual intercourse, whether they had multiple sexual partners, if they had genital herpes, whether they had ever smoked cigarettes, and whether or not they were currently smoking. Demographic characteristics associated with cervical cancer were also collected: age, years of formal education, race, and marital status.

If a woman reported anywhere on the questionnaire that she had a Pap smear in the last year, she was put into the Pap smear group. The remaining women went into the group without Pap smears. This latter group was further subdivided into two categories. One category included women who stated they did not see a physician for any reason during the last year; this category was identified as the "no opportunity" group. The other category was for the women without Pap smears who had seen a physician during the last year and was identified as the potential "missed opportunity" group.

Since hysterectomy is often considered a contraindication for Pap smear testing, the survey asked the women, "Have you ever had an operation to remove your uterus and/or ovaries?" Every possible combination of procedures was listed. Any response that included the removal of the uterus was used to determine hysterectomy status. Women who had a hysterectomy were not included in the analysis.

The chi-square statistic was used to test for differences among the three groups: the Pap smear group, the potential missed opportunity group, and the no opportunity group. A partitioned chi-square statistic was calculated as an independent test of differences between the two groups of women without Pap smears: the potential missed opportunity group and the no opportunity group.[9-11]

Results

Survey response. Of the 1,677 women in the sample, 68 could not be reached. More than 72% (N = 1,161) of the women who were contacted completed and returned their questionnaire. The 194 women who had a hysterectomy were removed from the analysis.

The distributions of all respondents by age and region of residence were compared to the sampling frame, the 1980 Census, and the group of nonrespondents and known refusals. Within several percentage points, the age distributions of respondents, the 1980 Census data, and the sampling frame were similar (Table I). However, black women and women with less than a high school education were underrepresented.

Table II describes the age and regional differences between respondents, nonrespondents, and the sampling frame (only available for age). The proportion of nonrespondents (including known refusals) was slightly higher among 35- to 44-year-old women and slightly lower among women aged 65 to 74. The distribution of respondents by geographic region were similar between the respondents and the nonrespondents.

Pap smear screening characteristics. Among women with intact uteri (N = 967), 97% stated that they had at least one Pap smear; 82% had one within the last three years; and 60% (N = 541) had one within the last 12 months (the latter being the Pap smear group, as defined above). Of the 40% who did not have a Pap smear within the last year, 21% (N = 185) reported that they had not seen a physician for any reason during that time (the "no opportunity" group). Nineteen percent (N = 169) had been to a physician at least once during the last year, but had not received a Pap smear during any of the visits (the potential "missed opportunity" group). Seventy-two respondents could not be classified by Pap smear group due to missing data.

Risk variables. Of the sample studied 21% stated that they had their first pregnancy under age 20. Fifty-one percent of the sample said they had their sexual debut before the age of 20. Furthermore, 21% reported multiple sexual partners and less than 1% reported a positive history of genital herpes. Of the women studied 57% reported that they had smoked cigarettes, while 30% indicated that they were currently smoking.

An additive index of these behavioral risk factors was constructed. This included the number of cumulative positive responses that were given to the above risk factors. The possible range of the risk index was between zero and six: 32% had no risk factors; 35% of the respondents had one factor; 26% had two factors; 6% had three factors; and less than 1% had four factors. None of the women had more than four of the risk factors.

Potential missed opportunities from physician visits. It was important that the potential missed opportunities be examined for all legitimate reasons why a Pap smear had not been provided during the physician visit. For 58% of the visits, the women reported that the physician seen did perform Pap smears. For 85% of the visits, the women stated that they were physically able to be screened. However, based on the respondent's definition of appropriate opportunities, only 10% of the visits were considered to be an appropriate opportunity for screening.

The potential missed opportunity group had 1.40 physician visits per person, which compared to an average of 1.54 among the Pap smear group. More women in the Pap smear group stated that the physician seen did Pap smear screening than women in the potential missed group (85% versus 58%). A few more in the Pap smear group stated that they were physically able to have a Pap smear done dur-

TABLE I. Comparison of Selected Sociodemographic Characteristics of Survey Respondents with 1980 Census Data Women, Aged 25–74, Upstate New York 1984

Group	1984 Survey respondents (%)*	1980 Census† (%)
Race		
White	95	92
Black	3	6
Other	3	2
Total	100	100
Education (years)		
8 or less	3	15
9–11	8	15
12	41	41
13 or more	48	30
Total	100	100
Marital status‡		
Married	71	54
Divorced	8	5
Separated	3	3
Widowed	9	13
Never married	10	26
Total	100	100
Age§		
25–34	31	26
35–44	23	21
45–54	16	19
55–64	17	19
65–74	13	14
Total	100	100

* Percents may not add to 100 due to rounding.

† Race, female all ages; education, aged 25 years or more; marital status, aged 15 years or more.

‡ Census data includes all women aged 15 years and older; survey respondents are aged 25 to 74 years. Thus differences in proportions are not strictly comparable.

§ From the Bureau of Biostatistics, New York State Department of Health, September 1982.

TABLE II. Comparison of Respondents to Nonrespondents By Age and Geographic Region of Residence Survey of Female Residents, Aged 25–74, Upstate New York 1984

Group	Respondents (%)	Nonrespondents (%)	Sampling frame* (%)
Age			
25–34	31	30	29
35–44	23	29	21
45–54	16	16	18
55–64	17	16	17
65–74	13	9	15†
Region of residence			
Long Island	26	31	NA
Other Downstate	11	13	NA
Northeast New York	17	19	NA
Central New York	17	15	NA
Western New York	28	22	NA
Total	100	100	100

* Licensed female drivers, upstate New York, Department of Motor Vehicles, 1980.
† Ages 65 years and older.
NA = Regional distribution of licensed drivers not readily available.

ing one of their visits as compared with the missed group (93% versus 85%). However, many more of the Pap smear group considered the visit to be an appropriate opportunity for Pap smear screening than did the potential missed group (64% versus 10%). Nearly three times as many women in the Pap smear group stated they were visiting the physician for a well-visit or check-up than were the missed group (44% versus 16%). The remaining 56% of the Pap smear group and 84% of the missed opportunity group stated that the reason for the physician visit was for illness.

When all of these factors were considered simultaneously—that is, the physician did Pap smears, the patient was physically able, and the visit was an appropriate opportunity—ten of the 169 potential missed opportunities seemed to be actual missed opportunities. These ten women represented about 1% of the total sample of women with intact uteri. The reasons for these ten visits included five women who were there for a check-up, one woman for hypertension, one for a gallbladder disorder, one for a gynecological problem, one for a thyroid ailment, and one for pregnancy.

The ages of the ten women with the missed opportunities from physician visits ranged from 27 to 71, with a median age of 51 years. All of the women were white. Eight of the women were married, one was widowed, and one had never been married. The total years of formal education ranged from 8 to 18, with the median number being 12.

Potential missed opportunities from hospitalizations. The New York State Health Code (10NYCRR 405.22) requires Pap smear screening for every female patient, 21 years or older, who is admitted to a hospital unless she is medically contraindicated or unless she has had a Pap smear within the past three years. The survey included questions regarding hospitalizations during the past year. A total of 18 hospitalizations were reported among the 169 potential missed opportunities.

The hospitalization rate per person in the potential missed group was .11, which was slightly lower than the Pap smear group at .19. For 53% of the visits, the women stated that it was not an emergency admission. The women reported that they were physically able to have the Pap smear done 76% of the time. However, the women stated that they had been asked whether they needed a Pap smear only 12% of the time. The reason for admission did not explain differential treatment with regard to Pap smear testing. Only three women admitted for pregnancy (delivery) and one of the five admitted for a heart condition considered themselves unable to have a Pap smear.

According to the regulations in the hospital code, the hospital was only required to provide uterine cytological examinations to those women who had not had a Pap smear within three years. Seven of the 18 visits fell into this category. One of these women was asked if she needed a Pap smear, while five of the seven stated they were physically able to have a Pap smear taken. Since these five women were different women from the ten physician visit missed opportunities, a total of 15 medical care contacts would be considered missed opportunities. This was 1.7% of the total number of women in the sample.

Comparison of groups by risk. The amount of concern generated over women who do not get Pap smears depends somewhat on their risk status. For example, if the known risk factors for cervical cancer cluster in the groups without Pap smears, then it may be assumed that the disease is even more likely to occur among these women who do not receive the benefits of early detection techniques.

Table III summarizes the sociodemographic risk factors among the potential missed opportunity, the no opportunity, and the Pap smear groups. No differences were detected among the three groups by race. Furthermore, no statistically significant differences among the three groups were noted by region of residence.

The differences by marital status showed that divorced and separated women were significantly more likely to be in the Pap smear group, while widowed women were most likely to be in the potential missed opportunity group. However, the partitioned chi-square analyses failed to detect any differences between the two groups of women without Pap smears.

Statistically significant differences by education were also detected among the three groups. Women with13 or more years of formal education were most likely to be in the Pap smear group. Furthermore, these differences by education were independent of age, as discussed by the authors elsewhere (unpublished data). A partitioned chi-square analysis between the two groups of women without Pap smears did not show any statistically significant differences.

Age was significantly related to the three groups. The contributions to the chi-square analysis were mostly from a concentration of 55- to 64-year-old women in the no opportunity group, 65- to 74-year-old women in the potential missed opportunity group, and 25- to 34-year-old women in the Pap smear group. The partitioned chi-square analysis for the two groups of women without Pap smears was also statistically significant. The differences between the two groups were primarily from the excess of potential missed opportunities among women aged 65 to 74 years.

The behavioral risk factors for the three groups are reported in Table IV. No statistically significant differences were detected for the risk factors of age at sexual debut, history of genital herpes, or cigarette smoking history. Statistically significant differences were noted for a history of multiple sexual partners; however, it was in the direction of those with the history being more likely to have had a Pap smear. The partitioned chi-square analysis did not show any differences between the two groups of women without Pap smears.

The variable, age at first pregnancy, revealed a statistically significant increase among women who were in the missed opportunity group. Women with a history of a pregnancy under the age of 20 years were more likely to have been to a physician and to have not received a Pap smear. The partitioned chi-square analysis between the two groups of women without Pap smears also showed a significant excess of these women to be in the potential missed opportunity group.

Current recommendations by the American Cancer Society are for triennial screening.[12,13] Although not shown in the Table, the data were examined for differences in risk factors between the respondents who had a Pap smear within three years and those who had not. No difference was detected by race; however, significant differences were noted by age, education, marital status, and behavioral risk factors. The variables of behavioral risk and education had a positive association while age had a negative one. Women who were either divorced or separated were the most likely to have received triennial screening.

Discussion

Data from an earlier survey were published[14] that suggested that missed opportunities could make a substantial

TABLE III. Percentage Distributions* of Sociodemographic Characteristics by Pap Smear Opportunity Group Women with Intact Uteri, Aged 25–74, Upstate New York 1984

	Papped group	Potential missed opportunity group	No opportunity group	Total (n)
Race				
White	61	19	20	845
Black	60	10	30	20
Hispanic	67	22	11	9
Oriental	50	—	50	6
Other	50	40	10	10
Marital status†				
Married	61	18	21	625
Divorced	70	18	11	71
Separated	74	7	19	27
Widowed	45	30	25	71
Never married	58	22	20	97
Education (years)‡				
9	41	32	27	22
9–11	43	24	33	58
12	53	22	25	355
13 or more	69	16	15	456
Age§				
25–34	71	15	14	313
35–44	58	17	25	217
45–54	52	22	26	130
55–64	51	21	29	122
65–74	50	34	16	88
Region of residence				
Long Island	57	19	24	242
Other Downstate	63	16	21	107
Northeast New York	63	17	19	149
Central New York	58	16	26	151
Western New York	62	23	15	243

* Percents may not add to 100 due to rounding.
† $\chi^2 = 16.37$, 8 *df*, $P < .05$.
‡ $\chi^2 = 36.15$, 6 *df*, $P < .0001$.
§ $\chi^2 = 40.36$, 8 *df*, $P < .0001$.

contribution to the proportion of women who have not received a recent Pap smear. This report studies the findings of a follow-up population survey on Pap smear screening utilization. The data for 1% of the sample were suggestive of actual missed opportunities in physician visits. When hospitalizations are added to this figure, total missed opportunities occurred for 1.7% of the sample studied. This percentage could indicate that a substantial number of visits are missed opportunities for uterine cytologic screening when applied to the total population.

In nearly all visits except those for pregnancy, the women felt that they were physically able to have a Pap smear. However, they also believed that for most of the visits it was not an appropriate opportunity. No explanation of inappropriate opportunities was asked. In the absence of corroborative information, a realistic expectation for Pap smear screening during any one medical visit was defined by the respondents.

The definition used here for actual missed opportunities in physician visits was conservative. It included three requirements: the physician did the screening, the woman was physically able, and she considered it an appropriate opportunity. Of the total sample 1% met these three requirements. If the definition was modified to include only that physicians could perform cytology screening on physically able women, 64% of the group of 169 women would have been defined as a missed opportunity (or 13% of the total sample). If missed opportunities were defined as occurring only among physically able women, then 154 of the 169, or 91% of the women would have been included (17% of the total sample). The proportion of potential missed opportunities, which did include any of the three conditions, complete the high end of the range of 19% potential missed opportunities. Regardless of definition, the actual numbers of women in the population affected by these proportions are sizable. Missed opportunities pose a significant problem to health care providers.

Black women, women who were 65 to 74 years of age, and women with less than 12 years of education were somewhat underrepresented in the sample. Since these demographic characteristics have been related negatively to Pap smear screening histories, they may suggest that the frequencies reported underestimate the true population frequencies of noncompliance with annual Pap smear screening.[15,16] Thus applying the rate of noncompliance identified in this research would provide a conservative estimate of the population need for screening services in upstate New York communities.

Several potential limitations of the study need to be addressed. One is that the Pap smear data are self-reported

and not validated by medical records. Meltzer and Hochstim[17] reported on the reliability and validity of survey data compared with medical records using data from the Human Population Laboratory. Although the two measures did not agree closely, they did find that the reasons were more related to methodological differences of the studies and had little relation to differences in recall, attempts at deception, or any other characteristics of the respondents.

The survey questionnaire did not directly measure the tendency to provide socially desirable responses. However, the tendency toward biased or incorrect recall may be evaluated in several ways. For example, Pap smear history for the preceding year was requested directly at the beginning of the questionnaire and then indirectly at the end of the questionnaire as part of the description of all visits to physicians during the same time period. The two Pap smear questions showed a high level of agreement. Only 18 responses did not agree out of a total of 944. The kappa statistic, which statistically measures the level of agreement that is not due to chance, was .95 (a score of perfect agreement would be 1.00).

Secondly, a number of "socially undesirable" questions were asked regarding risk factors for cervical cancer. These items included age at first pregnancy and at sexual debut and whether one had had multiple sex partners or genital herpes. They were revised for completeness of reporting and also for underreporting by comparison with other population estimates.

The item nonresponse for the questions on risk factors was less than 5% for any risk question. Specifically, data were missing for 3.3% on the age at first pregnancy question; 0.7% for the age at first intercourse question; 2.6% for the multiple sex partners question; 0.9% for the genital herpes question; and 0.6% on the question regarding current smoking status. In other population studies, it is generally quoted that 1% of all women under age 45 have genital herpes.

Population estimates for age at first pregnancy were obtained using reports from the Current Population Survey. These data would indicate that for comparable age groups in 1978, the proportion that would have had their first pregnancy under age 20 is similar for all age groups except those who were aged 35 to 39 years and 40 to 44 years in 1978.[18] For example, in the age group of women aged 40 to 44 years, our sample had 13% who fell into this category. However, the US Census data of 40 to 44 year old women showed that 25% of the US female population fell into this category. In the category of women 35 to 39 years of age, the sample had 24% while the US Census figures were 29%.

The possibility of bias from sample selection also needs to be considered. The sample was drawn from upstate New York female residents currently licensed to drive. It was determined that 91% of all upstate residents over the age of 18 have a current license to drive. This proportion was calculated using 1980 Census data for the upstate New York population over the age of 18 and using New York State Department of Motor Vehicles data on the number of active driver's licenses among upstate residents 18 years of age and older. If women alone were considered, this proportion might have been less, although prob-

TABLE IV. Percentage Distributions* of High Risk Variables to Cervical Cancer by Pap Smear Opportunity Group Women with Intact Uteri, Aged 25–74, Upstate New York 1984

	Papped Group	Potential missed opportunity group	No opportunity group	Total (n)
Age: first pregnant†				
19 or less	56	25	19	145
20–29	64	15	22	550
30 or older	54	26	19	57
Age: sexual debut‡				
19 or less	66	17	17	406
20–29	58	18	24	365
30 or older	47	27	27	15
Had multiple sex partners§				
Yes	74	13	13	200
No	56	21	23	674
Had genital herpes‖				
Yes	100	—	—	5
No	60	19	21	885
Current cigarette smoker‖				
Yes	57	20	23	271
No	62	19	20	623
Ever a cigarette smoker‖				
Yes	61	21	18	490
No	61	17	22	357

* Percents may not add to 100 due to rounding.
† χ^2 test, 4 *df*, $P < .05$.
‡ χ^2 test, 4 *df*, .05 $P < .10$.
§ χ^2 test, 2 *df*, $P < .0001$.
‖ χ^2 test, 2 *df*, not significant.

ably not dramatically different. This bias would only affect the interpretation of the data by underestimating the true prevalence of missed opportunities in the population of women living in upstate New York.

Fruchter and colleagues reported characteristics of missed opportunities in a low income community similar to those reported here. Low income and older women were more likely to be missed opportunities. They and Celentano and associates also reported that nonwhite women were more likely to be missed opportunities; however, our data did not support this finding.[20,21]

Several investigators have reported on programs for Pap smear screening that aim to take advantage of every medical contact by high risk women.[22-27] As a result of eliminating missed opportunities, the detection of cases increased; a shift from invasive to in situ cases was noted and a decrease in mortality resulted. Celantano and colleagues studied cervical cancer cases and found that the cases had more missed opportunities than their controls.[28]

The data reported here suggest a reassessment of appropriate opportunities for Pap smear screening. Older women tended to cluster in the potential missed opportunity group. Women who seem to have a number of symptoms or complaints that bring them into contact with a physician may feel that during this visit they have received a thorough check-up and do not require an additional well visit. Perhaps physicians also need to take advantage of all appointments, especially those of older patients, to insure that a Pap smear is included in at least one appointment in the year.

The triennial recommendations by the American Cancer Society could exacerbate this situation. This policy can reduce physician contacts and physician responsibility for ensuring that all women are adequately screened. Furthermore, it minimizes the chance that potential missed opportunities may become Pap smear opportunities.

From the other research and from the information reported here, the growing data base seems to indicate that expanding Pap smear screening into medical services, other than the traditional gynecologic examination, is a successful strategy for reaching generally high risk and unscreened women. It would certainly be in the interest of high risk women to transform the actual missed opportunities into screening opportunities. It may also be beneficial for physicians to indicate the importance of regular screening to all female patients; the physician should either take advantage of every medical visit and include Pap smear screening or refer the patient to a more appropriate provider when necessary.

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Metabolism of ethanol and associated interactions with other drugs, carcinogens, and vitamins

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Advances in the study of the metabolism of ethanol enable us to understand a number of clinically relevant interactions of the chemical with other drugs, carcinogens, and vitamins. The metabolism of ethanol is primarily hepatic and proceeds via three pathways, each located in a different subcellular compartment: the main pathway of alcohol dehydrogenase (ADH) in the cytosol (the soluble fraction of the cell); the microsomal ethanol oxidizing system (MEOS) in the endoplasmic reticulum; and catalase located in the peroxisomes. The latter pathway appears to be of limited importance, but the activation of ADH and MEOS may be associated with significant interactions with other drugs, carcinogens, and vitamins. Summarized here are the most clinically relevant interactions and the significant progress made since the publication of earlier reviews.[1-3]

PHARMACOLOGIC INTERACTIONS

The interactions between the pharmacologic effects of ethanol and those of other drugs at the primary site of action (particularly the central nervous system) is significant; they have been discussed elsewhere[4] and will not be reviewed here in detail in order not to exceed the scope of this article.

In addition to these pharmacologic effects, interactions between alcohol and other drugs may also occur at many other sites. Theoretically, alcohol consumption might alter drug absorption from the alimentary tract in a number of ways, notably by interfering with gastric emptying. The effective therapeutic level of a drug also depends on the degree of plasma protein binding. Hypoproteinemia may result in reduced plasma protein binding. Therefore, patients with alcoholic liver disease may be prone to developing toxicity from drugs such as quinidine, although plasma concentrations are in the usual "therapeutic" range. A major site of ethanol-drug interaction is the liver, either through interferences with flow, uptake, or metabolism. Hepatic metabolism may be affected in different ways, as outlined below.

INTERACTION OF ETHANOL WITH DRUG METABOLISM

A major advance in understanding the ways acute and chronic ethanol consumption modify drug handling by the body was brought about by the recognition of an accessory pathway of ethanol metabolism in the liver, namely the microsomal ethanol oxidizing system (MEOS).

Microsomal ethanol oxidizing system. Until recently, it was generally believed that the major pathway for ethanol metabolism involved hepatic cytosolic ADH (Fig 1A), with a minor contribution from peroxisomal catalase. Non-ADH ethanol oxidizing activity found in other subcellular fractions was usually attributed to a hydrogen peroxide-dependent reaction mediated by contaminating catalase, especially since this activity showed preference for methanol rather than ethanol, did not oxidize higher alcohols (such as butanol), and was exquisitely sensitive to catalase inhibitors.[5]

It had become known in the 1960s, however, that liver microsomes metabolize various xenobiotic agents (Fig 1A) and are capable of an adaptive enzymic response (enzyme induction) to drug administration, with proliferation of the membranes of the endoplasmic reticulum as a morphological counterpart. The observation in rats, as well as in man,[6] that chronic ethanol consumption is associated with such proliferation suggested that microsomes might also be a site of ethanol metabolism (Fig 1B), as subsequently documented.[7] Because of the properties of MEOS, including cofactor requirements and response to inhibitors, it was concluded that the microsomal hemoprotein cytochrome P-450 was involved.[7] This thesis stirred up a decade of extensive experimentation with lively and, at times, acrimonious debate.[5] The issue was finally settled after the following occurred: (1) The separation from the microsomes of a cytochrome P-450 containing a fraction devoid of ADH and catalase activity, but which contained the bulk of MEOS activity and could oxidize higher alcohols (such as butanol) that are not substrates for catalase.[8] (2) The reconstitution of the MEOS using NADPH cytochrome P-450 reductase, phospholipids, and cytochrome P-450.[9] (3) The demonstration of an ethanol-inducible form of cytochrome P-450 with high activi-

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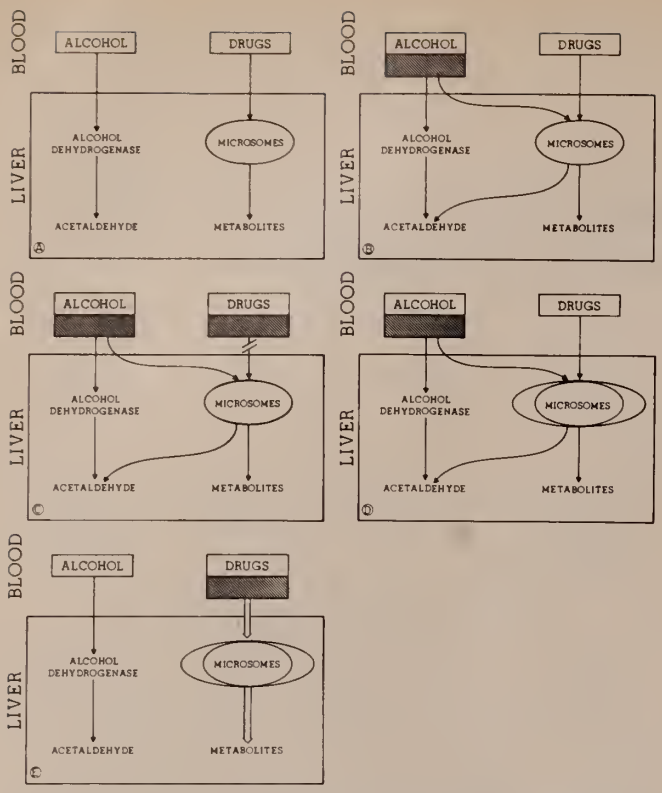

FIGURE. Schematic representation of hepatic alcohol-drug interactions involving the alcohol dehydrogenase pathway and the microsomes: (A) Metabolism of alcohol by ADH and drugs by microsomes; (B) Schematic representation of the contribution of the microsomal pathway to the metabolism of alcohol at increasing blood levels; (C) Inhibition of microsomal drug metabolism in the presence of alcohol, in part through competition for a common microsomal detoxification process; (D) Induction of microsomal activity after chronic alcohol consumption; (E) Accelerated drug metabolism because of microsomal induction after chronic alcohol consumption.

ty towards ethanol as a substrate.[9,10]

Several lines of evidence also support a role for MEOS in vivo, including the incomplete inhibition of ethanol metabolism using ADH inhibitors,[7,11] the pattern of labeling acetaldehyde derived from stereospecific labeled ethanol,[12] the increased rate of ethanol metabolism at high concentrations (well above those needed to saturate alcohol dehydrogenase), and the isotopic effect observed with deuterated ethanol.[13] Furthermore, the persistence of a substantial rate of ethanol metabolism in deer mice genetically devoid of hepatic ADH, in association with high MEOS activity,[14,15] illustrated the in vivo importance of non-ADH ethanol metabolism.

The contribution of MEOS to total ethanol metabolism in vivo has now also been determined in deer mice possessing liver ADH. By using ADH inhibitors, non-ADH pathways were found to contribute 39% of ethanol metabolism at a blood concentration of 10 mM ethanol (46 mg/dL) and 62% at 50 mM (230 mg/dL). From experiments using an approach involving the measurement of isotope effects, MEOS was calculated to account for 35% of the total ethanol oxidation at low ethanol levels and about 70% at high ethanol concentrations.[13] With a third approach, namely determination of the fate of ^{3}H removed from [1-^{3}H] ethanol during its metabolism, a contribution of non-ADH pathways to ethanol oxidation of up to 50% was found in rats.[16]

Elucidation of the MEOS pathway has improved the understanding of both the metabolic fate of ethanol and adaptation to its chronic consumption, and also of a number of interactions of ethanol with xenobiotics (Fig 1).

Acute interactions. The main effect of the acute presence of ethanol is the inhibition of hepatic drug metabolism (Fig 1C). One mechanism involved appears to be direct competition between ethanol and other drugs for a common metabolic process involving cytochrome P-450.[2] Ethanol may also interfere with microsomal drug metabolism indirectly by decreasing the supply of NADPH. Glucuronidation may also be affected: it was found to be inhibited by 50%.[17] In contrast, other drug detoxification processes such as acetylation[18] and sulfation[19] are unaltered by ethanol.

The acute interaction of ethanol with drug metabolism may have some important practical consequences. In the United States, more than 50% of all fatal road accidents are associated with an elevated blood alcohol level. One may wonder to what extent the loss of control on the road may be due not only to ethanol itself, but also to an ethanol-drug interaction, considering that a large segment of the population is given sedatives and tranquilizers. As reviewed elsewhere,[2] it has been shown that acute oral administration of ethanol results in prolongation of the clearance of meprobamate from the blood. Alcohol acts synergistically with meprobamate to depress performance tasks and driving-related skills such as time estimation, attention, reaction time, body steadiness, oculomotor control, and alertness.

Benzodiazepines are the most frequently used minor tranquilizers. Although earlier studies showed no synergism between alcohol and diazepam, the majority of recent investigations give clear indication that the combination is dangerous. The acute administration of ethanol also reduces the clearance of benzodiazepines of low intrinsic clearance (demoxepam).

The acute administration of ethanol in conjunction with phenothiazines may result in competitive inhibition of hepatic metabolism with decreased clearance and enhanced sedative effects. The use of phenothiazines to control symptoms of alcohol withdrawal may thus be hazardous. In addition, hypotension—a side effect of these drugs—may be exacerbated by alcohol.

Tricyclic antidepressants increase susceptibility to convulsions and therefore should be administered cautiously during alcohol withdrawal. Furthermore, since these drugs may produce hypotension, they should be prescribed only for alcoholics who can be carefully monitored. When combined with alcohol, tricyclic antidepressants adversely affect motor skills, particularly driving.

The combination of ethanol and barbiturates represents a particular danger. The lethal dose for barbiturates is nearly 50% lower in the presence of alcohol. Blood levels of secobarbital or pentobarbital as low as 0.5 mg/dL combined with blood levels of 100 mg/dL can cause death from respiratory collapse. A major reason for this is that alcohol inhibits the enzymes that metabolize barbiturates, so that the drugs are present in the blood stream in abnormally high amounts. Synergism and tolerance may occur

directly in brain tissue as well.

Ethanol also interacts with narcotics. Several epidemiologic studies suggest that the combined used of morphine and alcohol potentiates the effects of both drugs and increases the probability of death. Experimentally, acute administration of ethanol results in increased brain and liver concentrations of methadone.[20]

Acute ethanol intoxication reduces the metabolism of warfarin, leading to increased anticoagulant effects and the danger of hemorrhage. The combination causes blood warfarin levels to be higher than expected from a given dose. By contrast, chronic alcohol abuse may, by enhancing hepatic metabolism, lead to decreased anticoagulant effects of warfarin. Because the effects on prothrombin time can change with varying intake of alcohol, physicians need to monitor closely the prothrombin times in patients who drink.

Ethanol also interacts with industrial solvents. Occupational exposure to xylene is widespread in the manufacture and application of chemicals that contain xylene, notably paints, glues, printing inks, and pesticides. Alcoholic beverages are extensively consumed by some populations, occasionally in the course of the workday during lunch time and particularly after work. Since the excretion of xylene is delayed by its high solubility and storage in lipid-rich tissues, the simultaneous presence of xylene and ethanol in the body is most likely not uncommon. Indeed, after ethanol intake blood xylene levels were found to increase by about one and one half- to two-fold while urinary methylhippuric acid excretion fell by about 50%, suggesting that ethanol decreases the metabolic clearance of xylene by about one half during xylene inhalation.[21] Such an alteration in xylene pharmacokinetics is likely to be caused primarily by ethanol-mediated inhibition of hepatic xylene metabolism. Acute interactions of this type also have been described for other industrial solvents. Besides the enhancement of the toxicity of the parent compound, the presence of ethanol may also decrease the toxicity of certain solvents by the inhibition of the hepatic metabolism of a relatively innocuous parent compound to a toxic product. This is the case for carbon tetrachloride (CCl_4).[22]

Although most acute ethanol-xenobiotic interactions involve alterations in the disposition of such compounds by ethanol, the converse may also occur. For instance, it has been reported that ethanol metabolism may be affected by oral administration of cimetidine at therapeutic doses,[23] although this has recently been disputed.[24]

Chronic interactions. It is well known that chronic alcohol abusers develop tolerance to ethanol. Such tolerance is due, in part, to central nervous system adaptation (pharmacodynamic tolerance). In addition, there is also metabolic tolerance that results from an increased capacity to oxidize ethanol. This occurs because of the adaptive increase in activity of non-ADH pathways involved in ethanol metabolism, most likely MEOS as discussed earlier (Fig 1D).

In addition to tolerance to ethanol, alcoholics also tend to display tolerance to various other drugs; this has been generally attributed to central nervous system adaptation. However, metabolic adaptation must also be considered. Indeed, the induction in the activity of MEOS after chronic alcohol consumption "spills over" to various other drug-metabolizing systems in liver microsomes, thereby accelerating drug metabolism in general (Fig 1E). As a consequence, the administration of ethanol to man under metabolic ward conditions resulted in a striking increase in the rate of blood clearance of meprobamate and pentobarbital.[25] Similarly, increases in the metabolism of aminopyrine, tolbutamide, propranolol, and rifampicin due to ethanol administration have been described. Experimentally, this effect of chronic ethanol consumption may be modulated in part by the dietary content in carbohydrates,[26] lipids,[27] and proteins.[28]

Thus, a recovered alcoholic's previous history of alcohol abuse may be a key factor in prescribing medication, because even abstaining alcoholics need doses different from those required by nondrinkers to achieve therapeutic levels of certain drugs, such as warfarin, phenytoin, tolbutamide, and isoniazid. The half-life of each of these drugs may be 50% shorter in abstaining alcoholics than in nondrinkers; this metabolic tolerance will persist several days to weeks after cessation of alcohol abuse, and the duration of recovery varies depending on the drug considered.[29] These agents may have to be prescribed in increased amounts for patients in the recovery phase of alcoholism. This applies to those drugs to which alcohol produces pharmacologic as well as metabolic tolerance, such as diphenylhydantoin, barbiturates, benzodiazepines, tolbutamide, propranolol, and rifamycin.

Chronic alcohol intake has been determined to enhance susceptibility to hepatotoxic agents. The general increase in microsomal enzyme activities also applies to those that convert exogenous substrates to toxic compounds. For instance, CCl_4 exerts its toxicity after conversion to an active metabolite in the microsomes, and alcohol pretreatment remarkably enhances CCl_4 hepatotoxicity.[30] Thus, the clinical observation of the enhanced susceptibility of alcoholics to the hepatotoxic effect of CCl_4 may be due, at least in part, to increased metabolic activation of this compound. Liver toxicity of bromobenzene was also found to be increased following chronic alcohol consumption.[31] It is likely that a large number of other toxic agents will be found to display a selective injurious action in the alcoholic patient. This pertains not only to industrial solvents, but also to a variety of prescribed drugs. For instance, the increased hepatotoxicity of isoniazid observed in alcoholics may well be due to increased microsomal production of an active metabolite of the acetyl derivative of the drug. Similarly, chronic ethanol administration enhances phenylbutazone hepatotoxicity, possibly because of increased biotransformation.[32]

The same mechanism of hepatotoxicity also pertains to some over-the-counter medications. Acetaminophen (paracetamol, N-acetyl-p-aminophenol), widely used as an analgesic and an antipyretic, is generally safe when taken in recommended doses. However, large doses of acetaminophen, most often taken in suicide attempts, have been shown to produce fulminant hepatic failure. It is now clear that in addition to glucuronidation and sulfation, acetaminophen is also metabolized in the liver by the microsomal cytochrome P-450 system; the latter biotransformation yields an active metabolite highly toxic to the liver. The practical implications are obvious in view of the widespread use of drugs known to be inducers of microsomal

drug metabolizing activities. Because alcohol may also induce microsomal drug metabolizing systems, it was to be expected that a history of alcohol consumption might favor the hepatotoxicity of acetaminophen. This has been suggested in various case reports.[33] Experimentally, after chronic ethanol feeding, enhanced covalent binding of reactive metabolite(s) of acetaminophen to liver microsomes from rats was observed to be associated with enhanced hepatotoxicity.[34] Furthermore, in a reconstituted system, an ethanol-inducible form of cytochrome P-450 was found to have a high capacity to oxidize acetaminophen to a reactive intermediate that readily formed a conjugate with reduced glutathione.[35] It is therefore likely that the enhanced hepatotoxicity of acetaminophen observed after chronic ethanol consumption is due, at least in part, to increased microsomal production of such reactive metabolite(s) of acetaminophen. However, unlike pretreatment with alcohol, which accentuates toxicity, the presence of ethanol in part prevents the acetaminophen-induced hepatoxicity, most likely because of inhibition of the biotransformation of acetaminophen to reactive metabolites.[36-38] This type of interaction is similar to that described for other drugs. The extent to which ethanol competes with the microsomal metabolism of acetaminophen still remains to be evaluated.

Alcohol abuse has also been associated with an increased incidence of upper alimentary and respiratory tract cancers. Many factors have been incriminated in the cocarcinogenic effect of ethanol.[1] One of the mechanisms is believed to be the effects of ethanol on enzyme systems involved in carcinogen activation. The effect of ethanol on cytochrome P-450 dependent carcinogen activation has been demonstrated using microsomes derived from a variety of tissues including the liver (the principal site of xenobiotic metabolism), the lungs and intestines (the major portals of entry for tobacco smoke and dietary carcinogens, respectively), and the esophagus (where ethanol consumption is a major risk factor in cancer development).[39-41] The general approach used in these studies has been to isolate microsomes from tissues of ethanol-exposed rats, hamsters, or mice and then assay these preparations for their ability either to metabolically activate procarcinogens to mutagens detectable in the Ames Salmonella mutagenesis assay or to produce defined products. Ethanol also has a unique effect on the chemical carcinogen dimethylnitrosamine (DMN): it induces microsomal DMN N-demethylase activity that functions at low DMN concentrations.[42] This is in contrast to other microsomal enzyme inducers such as phenobarbital, 3-methylcholanthrene, and polychlorinated biphenyls. These compounds increase the activity of DMN N-demethylases—the activity of which is detectable only at relatively high DMN concentrations—while repressing the activity of DMN N-demethylases active at low concentrations.[43] Some of these effects may be due to the induction of a unique species of cytochrome P-450 by ethanol as described earlier,[9,10] which differentially affects the activation of various carcinogens; indeed a selective affinity for DMN has been demonstrated with the ethanol-induced form of cytochrome P-450.[44]

Ethanol also affects microsomal metabolism of exogenous and endogenous steroids, as discussed in detail elsewhere[2]; the effects include enhanced testosterone degradation and conversion to estrogens, as well as decreased testicular steroid synthesis. Furthermore, ethanol alters the metabolism of structurally related vitamins, such as vitamin D.[45] These and other micronutrients may serve as substrates for the microsomes, and the induction of the microsomal oxidative activities therefore may alter vitamin requirements and even affect the integrity of the liver and other tissues. It had been known that plasma vitamin A, as well as retinol-binding protein (RBP) levels,[46] are decreased in patients with alcoholic cirrhosis. These complications have usually been attributed either to malnutrition or to hepatic injury, because decreased plasma vitamin A and RBP levels have been reported in patients with liver disease without apparent alcohol intake.[47] Inadequate dietary intake of zinc, increased urinary zinc loss, and depressed serum zinc levels are common in chronic alcoholics with or without liver diseases.[48] Alcoholic cirrhosis is often associated with zinc deficiency, which has also been postulated to decrease plasma RBP through impaired mobilization of RBP from the liver. In addition, it has been found recently that at the early fatty liver stage, alcoholics commonly have very low hepatic vitamin A levels despite normal circulating vitamin A and the absence of obvious dietary vitamin A deficiency.[49] In experimental animals, ethanol administration was shown to depress hepatic vitamin A levels, even when administered with diets containing adequate amounts of vitamin A.[50] When vitamin A was virtually eliminated from the diet, the depletion rate of hepatic vitamin A stores was two to three times faster in ethanol-fed rats than in controls, possibly because of accelerated microsomal degradation of vitamin A.[51] Furthermore, it has been shown by using reconstituted systems with purified forms of cytochrome P-450, that retinoic acid may serve as a substrate for microsomal oxidation.[52] An even greater microsomal metabolism was found for retinol. Indeed, a new pathway of microsomal retinol metabolism has been discovered in the liver, inducible by either ethanol or drug administration, and capable of degrading an amount of retinol comparable to the daily intake.[53]

For all of these reasons, vitamin A supplementation should be given not only to correct the problems of night blindness and sexual dysfunction of the alcoholic, but such therapy might also be useful with regard to liver dysfunction. Indeed, low hepatic vitamin A levels might be responsible for some functional or structural abnormalities in the liver, including giant lysosomes.[54] Vitamin A depletion may also result in mucosal alterations and indirectly favor enhanced carcinogenesis.[55] The therapeutic administration of vitamin A, however, is complicated by the fact that excessive amounts of this vitamin are known to be hepatotoxic and that the alcoholic patient has an enhanced susceptibility to this effect.[56,57] In control rats, amounts of vitamin A equivalent to those commonly used for the treatment of the alcoholic did not have significant toxic effects on the liver. However, signs of toxicity developed in animals chronically fed alcohol, such as striking morphologic and functional alterations of the mitochondria,[56] along with necrosis and fibrosis.[57] Enhanced toxicity was not necessarily associated with an increased vitamin A level in the liver. In fact, because alcohol

administration tends to decrease vitamin A levels in the liver, even after supplementation, some alcohol-fed animals had vitamin A levels in the liver that were not higher than normal.[56] Toxicity developed nevertheless. One possible explanation that has yet to be proven is that vitamin A toxicity may be mediated, at least in part, by the enhanced production of a toxic metabolite, as in the case of certain xenobiotic agents. In any event, further studies will be needed to more clearly define the narrowed "therapeutic window" for vitamin A in the alcoholic patient. The practical implications of these considerations are obvious.

Due to poor dietary intake and in some instances malabsorption and lack of activation, vitamin deficiencies are relatively frequent in the alcoholic and vitamin supplementation is commonly practiced, whether deficiencies are present or not. Such an approach to therapy may be harmless, as in the case of some water soluble vitamins (ie, thiamine and folic acid). However, not all water soluble vitamins are harmless when taken in excess. Indeed, pyridoxine toxicity has been described in the literature.[58] Caution is also needed in the administration of some lipid soluble vitamins. Indication for vitamin A supplementation in the alcoholic patient may be expanded from hypogonadism and night blindness to possible correction of liver dysfunction. As discussed before, however, vitamin A therapy is complicated by its potential hepatotoxicity, which was found to be enhanced after chronic alcohol consumption. Large amounts of vitamin A, such as 100,000 IU daily (recommended for the nonspecific treatment of Crohn's disease[59]) are dangerous in the heavy drinker; a 50 times lesser dose is more in keeping with proper nutritional replenishment while avoiding toxicity.

Reactions Between Ethanol and Other Alcohols

In addition to ethanol, a number of other alcohols may serve as substrates for ADH. This pathway is particularly important when the product formed is highly toxic, as in the case of ethylene glycol. This compound, commonly used as a solvent and in antifreeze solutions, is oxidized by ADH to its corresponding aldehyde and then to the highly toxic oxalic acid. Ethanol may be used to competitively inhibit ethylene glycol oxidation by ADH, so that the compound is gradually excreted unchanged. Indeed, ethanol therapy has been found to be effective in cases of ethylene glycol poisoning.

Methanol poisoning may also be treated with ethanol. A dose sufficient to keep the level of ethanol in the blood between 100 and 150 mg/dL is recommended. 4-Methylpyrazole, which inhibits both ADH and MEOS, has also been proposed for such therapeutic use.

Reactions Involving Acetaldehyde

Acetaldehyde is produced from ethanol in all of its hepatic pathways. It is highly toxic and is rapidly metabolized by aldehyde dehydrogenase. Inhibition of this enzyme by disulfiram has clinical application in the aversive treatment of some alcoholic patients. The full disulfiram reaction is due partly to acetaldehyde retention and partly to an inhibition of dopamine oxidase, which results in lowered tissue levels of norepinephrine.

When taken with alcohol, some drugs inhibit acetaldehyde metabolism and cause an acute disulfiram-like reaction with nausea, headache, vomiting, and possibly convulsions. Such agents include the sulfonylureas, chloramphenicol, furazolidone, griseofulvin, metronidazole, and quinacrine. The reactions produced by these agents are generally less severe than those produced by disulfiram.

Interactions with Congeners

Acetaldehyde does not only result from ethanol metabolism in the body but is also present as a congener in various alcoholic beverages. Alcoholic beverages may also contain a variety of other congeners, which in turn may interact with the effect and metabolism of a number of drugs. Some types of beer and wine, for instance, contain tyramine; some types of beer also contain dihydroxyphenylalanine. These compounds may precipitate a hypertensive crisis in patients treated with monoamine oxidase (MAO) inhibitors. Indeed, tyramine is a pressor amine that releases norepinephrine from the tissues. In the presence of MAO inhibitors, the degradation of tyramine is blocked and the enhanced tissue level of tyramine results in greater release of norepinephrine. Dopa is a precursor of dopamine, and its accumulation produces effects similar to those produced by tyramine. Not all alcoholic beverages have been implicated in hypertensive reactions with MAO inhibitors. However, because of the variability in the nonethanol components of alcoholic beverages, and in order to avoid confusion on the part of patients receiving these drugs, they should be advised against taking alcoholic drinks at all.

As a general rule, altered doses of prescribed drugs are not indicated in patients with compensated alcoholic liver disease. However, a reduction in dosage is frequently indicated in patients with decompensated hepatic disease (ie, clinically evident alcoholic hepatitis or advanced cirrhosis). Furthermore, the enhanced susceptibility of these patients to coma when they are taking central nervous system depressants or diuretics should also be considered. The interactions of liver disease, alcohol, malnutrition, and drugs have been reviewed in detail by other researchers.[60]

In conclusion, recent advances in studies of the metabolism of ethanol have resulted not only in elucidation of various mechanisms of hepatotoxicity[61] but also in a better understanding of acute and chronic interactions of ethanol with other drugs, carcinogens, and vitamins. The discovery of a cytochrome P-450 dependent pathway of ethanol metabolism in liver microsomes explains how ethanol may interact acutely with the metabolism and effects of many commonly used drugs, whereas the induction of liver microsomes secondary to chronic ethanol consumption explains, in part, the tolerance of the alcoholic to a variety of therapeutic agents. Microsomal induction may also result in the enhanced activation and toxicity of some drugs and industrial solvents; it also results in the accelerated degradation of steroids and vitamins. These various interactions have a significant impact on nutritional supplementation and commonly used medications that may be affected by, or interact with, either ethanol or acetaldehyde metabolism. The ethanol induced form of cytochrome P-450 was also found to have an unusual capacity

to activate carcinogens, a mechanism that may contribute to the enhanced incidence of cancer in the alcoholic.

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Clinical conference on tuberculosis and sarcoidosis

Case Presentation

Dinesh Samayamantri, MD (Intern, Department of Medicine): A 49-year-old woman was admitted to the hospital with cough, purulent sputum, low grade fever, and loss of appetite for three weeks. Sarcoidosis was diagnosed four years earlier by skin biopsy. Subsequently, intermittent recurrent pain occurred in the left shoulder, left wrist, and left hand; this was treated with naproxen. Two years prior to the present admission, a liver biopsy precipitated by abnormal liver function tests demonstrated noncaseating granulomata. No steroid treatment was given.

Three weeks prior to admission, the patient developed fever, cough, and purulent sputum; chest radiograph revealed a consolidation in the upper lobe of the left lung. Treatment with erythromycin was ineffective.

Physical examination on admission to the hospital revealed pallor and weight loss. Blood pressure was 100/60 mm Hg; pulse rate, 100/min; respiratory rate, 18/min; and temperature, 100°F by rectum. Discrete, small, nontender lymph nodes were palpable throughout. Ocular examination was normal. Increased vocal fremitus and resonance were noted over the left upper lung field, with bronchial breath sounds in the left infraclavicular region and amphoric breathing in the left suprascapular region. A grade 2/6 systolic murmur was loudest at the apex but audible over the entire precordium. By percussion, the liver span was 20 cm; the edge was nontender and smooth. The spleen edge was 4 to 5 cm below the left costal margin. Neurological examination and ECG were normal.

Urine analysis showed a one-plus test for protein and 15 to 20 WBCs per high power field, with no bacteria on Gram stain. The hemoglobin level was 11.9 g/dL; hematocrit, 35.1%; WBC count, 5,800/μL, with a normal differential count. Red blood cell indices, platelet count, prothrombin time (PT), and partial thromboplastin time (PTT) were normal; routine blood cultures were negative. The following chemical determinations were normal: serum electrolytes, calcium, creatinine, BUN, serum angiotensin-converting enzyme, and arterial blood gas levels. Serum cholesterol levels ranged between 260 mg/dL and 403 mg/dL. Gamma-glutamyl transpeptidase (GGTP) levels were markedly elevated at 327 U (normal, less than 35 U).

On the second hospital day, the sputum smear was positive for acid-fast bacilli; treatment with isoniazid and rifampin was initiated. The fever persisted, and acid-fast bacteria remained visible on the sputum smear. The serum bilirubin level rose from 0.5 mg/dL to 3 to 4 mg/dL; SGOT was intermittently elevated, as high as 132 U/L; lactate dehydrogenase (LDH) was persistently elevated between 173 U/L and 265 U/L; and serum alkaline phosphatase levels rose from 371 U/L to 1,120 U/L.

Fluid aspirated from the left wrist area revealed 73 polymorphonuclear leukocytes and 40 lymphocytes/μL; no acid-fast bacteria were seen on stained smear. A synovial biopsy was then considered.

John Batillas, MD (Attending Physician, Department of Radiology): The chest radiograph taken one year prior to admission showed increased markings toward both lung

FIGURE 1. Posteroanterior view of chest one year prior to admission showing increased bronchovascular markings at both lung bases.

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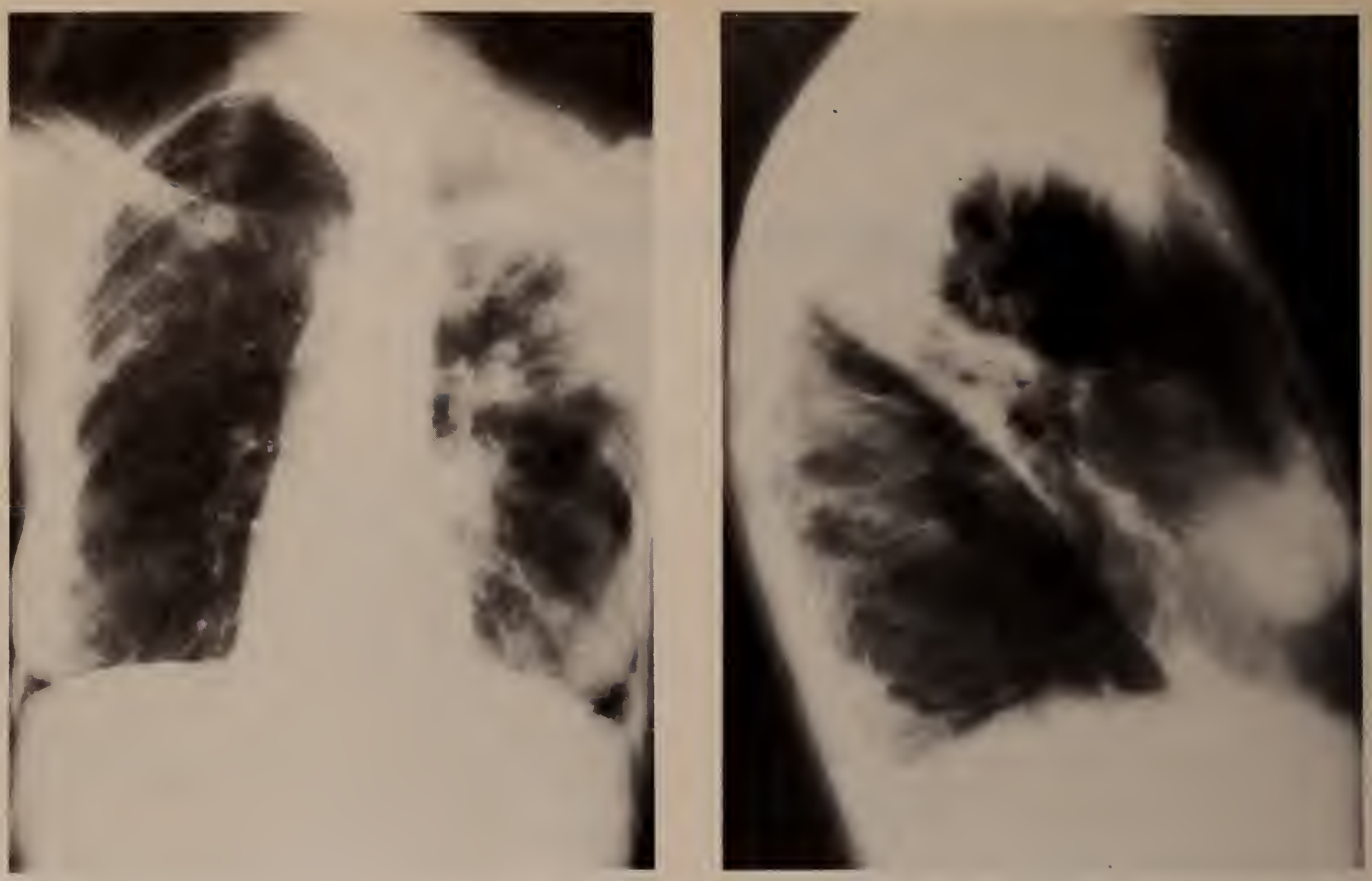

FIGURE 2. Posteroanterior (left) and left lateral (right) views of chest on admission showing bilateral upper lobe infiltrates and large cavity in posterior segment of left upper lobe.

bases but no hilar adenopathy or infiltrations (Fig 1). However, the chest films taken on admission demonstrated bilateral upper lobe infiltrates, more on the left, with a large cavitary lesion in the posterior segment of the left upper lobe (Fig 2).

A sonogram taken of the right upper quadrant documented the hepatosplenomegaly but showed no biliary tract dilatation. A liver-spleen scan revealed moderate splenomegaly and massive hepatomegaly with heterogeneous distribution of radionuclide material compatible with diffuse hepatocellular disease. A space-occupying hepatic lesion could not be ruled out. Films of the hands and feet (Figs 3 and 4) show the characteristic reticular pattern of sarcoidosis in the carpal, metacarpal, and metatarsal bones and in the toes. The distal phalanx of the left thumb was the site of a pathologic fracture.

Irwin Sharkey, MD (Chief, Department of Medicine): Was the serum alkaline phosphatase fractionated?

Dr Samayamantri: Yes, the increase was predominantly in the hepatic fraction.

Dr Sharkey: What did the synovial fluid reveal other than the white blood cells?

Charles Lebowitz, MD (Chief Resident, Department of Medicine): Only a few birefringent crystals were noted under the polarizing microscope. The smear for acid-fast bacilli was negative.

Dr Sharkey: What was the patient's blood uric acid level?

Dr Lebowitz: The level ranged from 4.3 mg/dL to 8.0 mg/dL.

Dr Sharkey: Do the bone changes as determined on radiographic examination suggest gout in any way?

Dr Batillas: No, the changes appear much more compatible with sarcoidosis.

Diagnostic Aspects of Sarcoidosis Versus Tuberculosis

Donald Woodburn, MD (Resident, Department of Medicine): Sarcoidosis is a diagnosis of exclusion based on granulomatous involvement of two or more tissues, no other proven cause of granulomatous disease, and clinical findings that support the diagnosis. The initial evidence of pulmonary sarcoidosis is an alveolar infiltrate of activated T-lymphocytes and mononuclear phagocytic cells,[1] reaching a peak before formation of the granulomata and thereafter diminishing.

Bilateral hilar adenopathy (BHL), erythema nodosum, parotitis, and uveitis are hallmarks of sarcoidosis.[2] However, BHL occurs in only about 38% of patients with the disease and can accompany miliary tuberculosis and the inhalation of organic and inorganic dusts.[3]

To most clinicians, caseation in granulomas is indicative of tuberculosis; however, similar necrotic granulomatous tissue is found in other bacterial, fungal, spirochetal, and neoplastic diseases.[4] Sarcoid granulomas may undergo eosinophilic granular necrosis, but generally retain their usual architecture.[5] Acid-fast rods that are not mycobacteria may be seen in noncaseating sarcoid granulomas[6-9]; proof of mycobacterial infection requires positive cultures from tissue specimens.

FIGURE 3. Reticular pattern of bone trabeculae, typical of sarcoidosis, involving left thumb (top), and proximal phalanx, left third finger (bottom).

The lymph nodes that drain a pulmonary neoplasm may contain a few scattered, poorly-formed granulomas.[10,11] Sarcoid granulomatous invasion of the walls of blood vessels may be mistaken for primary granulomatous arteritis.[4]

Asymptomatic BHL without physical findings, or BHL with erythema nodosum or uveitis, strongly favors sarcoidosis; biopsy ordinarily is not needed.[12] However, biopsy is necessary when BHL is associated with pleural effusion, an anterior mediastinal mass, parenchymatous pulmonary nodules, peripheral lymphadenopathy, hepatosplenomegaly, unexplained anemia, an infiltrative skin rash, or suspected neoplasm.

To prove beyond a doubt that granulomas represented sarcoidosis, the pathologist would have to employ polarized light microscopy, histochemical and incineration techniques, spectography, microsound, and radiographic diffusion techniques in order to exclude the presence of bacteria, fungi, parasites, and foreign particles such as silica, cement, synthetic fibers, wood particles, and certain plastics. Ordinarily the diagnosis of sarcoidosis depends on biopsy of glandular, dermal, or pulmonary lesions, together with an exhaustive environmental and occupational history.

When the chest radiograph is normal, histologic evidence from more than one site should be secured. Positive biopsy specimens from mediastinal nodes are obtained from 99% of patients with sarcoidosis; negative biopsy results practically exclude that diagnosis.[13] With adenopathy alone, transbronchial lung biopsy secures positive tissue in 60% of patients with sarcoidosis and in 93% of patients with pulmonary infiltrates. Bronchoscopy may uncover other diagnoses as well.[14,15] Transbronchial lung biopsy should precede open lung biopsy or mediastinoscopy, whenever one or the other of the latter two tests appear necessary.[4]

Bronchial mucosa, conjunctiva, and skeletal muscle contain demonstrable granulomas in 10% to 30% of patients with sarcoidosis.[16] In 50% to 80% of patients with the disease extensive search will eventually demonstrate thinly scattered granulomas in skeletal muscle.[17] When found, the granulomas offer strong support for sarcoidosis. Negative muscle biopsy specimens are inconclusive.

Liver biopsy demonstrates granulomas in 80% of patients with sarcoidosis. However, noncaseating hepatic granulomas may occur with a host of bacterial, spirochetal, viral, and fungal infections. These granulomas may also occur with dust inhalations, immune deficiencies, malignant tumors, inflammatory bowel disease, and primary biliary cirrhosis.[2,6,18]

In the setting of disseminated tuberculosis, needle biopsy will demonstrate mycobacteria in only 10% of hepatic granulomas,[19] and little or no caseation unless the dissemination is overwhelming.[20,21] In most cases mycobacteria must be isolated from other organs.

The histologic appearance of hepatic granulomas usually does not pinpoint the underlying cause, with the exceptions of schistosomiasis, visceral larvae migrans, granulomatous arteritis, and starch granulomas.[19]

The liver may harbor millions of granulomas with sarcoidosis. Yet only 15% of patients with the disease have abnormal liver function tests. These granulomas may disappear rapidly or persist for many years despite prolonged corticosteroid therapy.

Where extensive clinical study fails to identify the cause of hepatic granulomas, mediastinoscopy with lymph node biopsy is considered the best method to either establish or rule out sarcoidosis. The clinical accuracy of the Kveim test has improved. With suitably prepared antigen and proper administration, 97% of patients with sarcoidosis have positive Kveim tests. One disadvantage to the Kveim test, however, is that the test material is not widely available.

When positive for sarcoidosis a papular nodular lesion

with well-formed epitheloid tubercules will appear within several weeks after the intracutaneous injection of sarcoid tissue. This is more likely to occur with lymph node and skin manifestations, and less likely in the absence of adenopathy or during steroid therapy. The response diminishes with increased duration of the sarcoidosis. When granulomas are found in one organ, such as the liver, a positive Kveim test indicates that sarcoid granulomas are present elsewhere.[5]

Occasionally false-positive reactions on the Kveim test occur in the presence of inflammatory bowel disease and diseases of the lymphatic system.[5,22]

Two thirds of patients with sarcoidosis in an acute phase have increased serum angiotensin-converting enzyme (ACE); however, less than one half of those patients with long-standing sarcoidosis will have an elevation. The ACE level may also be elevated in other infections, granulomatous diseases, and in pulmonary conditions.[23] Rapid reduction in ACE levels occurs within the first two to three weeks of steroid therapy for sarcoidosis.

In sarcoidosis, increased numbers of T-lymphocytes in bronchoalveolar lavage fluid help to indicate the intensity of sarcoid alveolitis, the stage of the disease, and the response to therapy.[22]

Gallium-67 binds to inflammatory granulocytes. Abnormal pulmonary Gallium-67 scans were found in 97% of patients with clinically active sarcoidosis, and in 71% of patients with clinically inactive disease. Thus, reversion to a negative Gallium-67 scan occurs with a subsiding phase of pulmonary sarcoidosis,[24] or with prednisone therapy.[25]

When sarcoidosis is already strongly suspected, a positive gallium scan of the lungs offers further support, especially with simultaneous increased uptake in the parotid and lacrimal glands and in other tissues. Positive thoracic Gallium-67 scans are also seen in many other conditions, and are not specific for sarcoidosis.

Acute or chronic arthritis occurs in about 15% of patients with sarcoidosis.[26] The chronic form may develop at any time, and may lead to joint destruction. Granulomas are present in the synovia but radiographs of the joints are often negative. This was true for our patient; in spite of long-standing arthritic complaints, her films showed only the classical bone changes of sarcoidosis.

The overall course of sarcoidosis tends to be benign. At the end of a two- to 20-year follow-up of 125 patients, 87% were well, 3% were disabled by pulmonary disease, and 10% had died, primarily of respiratory failure.[27] With this high frequency of spontaneous recovery, any long-term treatment is difficult to evaluate. But in the short term, steroids can markedly slow the progress of fulminant disease, improve lung volume, relieve dyspnea, and shrink pulmonary infiltrates; diffusing capacity may remain low, however. Steroid therapy apparently does not increase the incidence of infections in sarcoidosis, but reduction of steroid dosage may lead to relapses and return of symptoms.[5]

Michael Davis, MD (Chief Resident, Department of Medicine): I wish to review briefly some of the more complex relationships of tuberculosis with sarcoidosis.

Autopsy studies indicate a 15 to 20% incidence of tuberculosis in sarcoidosis[28]; but in clinical studies, the incidence is less than 1%.[29] Tuberculosis is common among American-Chinese, American Eskimos, and American Indians, while sarcoidosis is rare[14]; both are common in blacks.

FIGURE 4. Reticular pattern of bone trabeculae involving the toes.

In the setting of tuberculosis, hypersensitivity to intradermal tuberculin develops two to ten weeks after primary infection, and may be followed by pulmonary fibrosis and caseation necrosis. Most patients with active tuberculosis, unless moribund due to overwhelming disease, react to intermediate-strength tuberculin tests (5 U); 90% will react to second-strength tuberculin (250 U) when proper test techniques are observed. Patients with sarcoidosis complicated by tuberculosis also tend to react to second-strength tuberculin. A negative second-strength (250 U) tuberculin skin test is strong evidence against a tuberculous cause of hepatic granulomas.[6]

The appearance of anergy to tuberculin may result from inadequate test materials, poor testing technique, lack of prior exposure to tuberculosis, intercurrent skin disease, several types of vaccinations, measles, anticoagulant therapy, intercurrent metabolic and nutritional diseases, immediate hypersensitivity reaction at the test site, immunosuppressive therapy, or surgery within the preceding two weeks.[30]

Sensitivity to tuberculin, which develops normally after bacille Calmette Guerin vaccine, vanishes when sarcoidosis supervenes and returns either after recovery from the disease[31] or with steroid therapy. Patients with sarcoidosis who are anergic to tuberculin retain a normal ability to reject skin homografts, which is not usually true in the immunocompromised patient with Hodgkins disease.[5]

Thus, an inherent defect in cell-mediated immunity does not appear to be a prerequisite for the development of sarcoidosis.

Antituberculous drug treatment has little influence on the course of sarcoidosis, suggesting an etiology other than *Mycobacterium tuberculosis*. I would also like to add a few words on this type of treatment.

Streptomycin is bacteriocidal in slightly alkaline media for rapidly multiplying extracellular tubercle bacilli; isoniazid (INH) and rifampin are bacteriocidal for extracellular and intramacrophage bacilli; and pyrazinamide is bacteriocidal for bacilli in closed cavities and within macrophages.

When a patient's tubercle bacilli were initially resistant to INH or became resistant because of inappropriate past use of the drug, treatment should include streptomycin, pyrazinamide, rifampin, and INH during the first six to eight weeks, or until drug susceptibility tests indicate the need to modify therapy.

Ethambutol, ethionamide, cycloserine, and para-aminosalicylic acid (PAS) are bacteriostatic; they replace bactericidal drugs only when two or more of the latter produce significant adverse reactions or when resistant organisms appear. Longer regimens up to 24 months are required when bacteriostatic drugs are used under these circumstances.

I would like to bring to your attention an important study.[32] Kent and his colleagues at the St Albans Naval Hospital addressed the following question: How reliable is the diagnosis of sarcoidosis when based on clinical findings, radiographic abnormalities, and a peripheral tissue biopsy compatible with that diagnosis, but without other investigative procedures?

A total of 30 patients, all active duty military personnel or their relatives, presented with clinical and roentgenographic findings compatible with sarcoidosis, together with biopsy specimens of scalene fat pad or other peripheral tissues that revealed "noncaseating granuloma consistent with the diagnosis of Boeck's sarcoid." Skin tests, cultures, and cytologic and serologic studies were all negative for infectious granulomatous disease and tumor.

All of the patients underwent diagnostic thoracotomy; biopsy specimens of the pleura, lung, and mediastinal lymph nodes were subjected to histologic, cytochemical, and cultural studies.

Tuberculosis was established in 19 instances—by lung biopsy in eight patients; by sputum cultures in three; and by culture of joint fluid in one. In two patients, scalene fat pad biopsy specimens were positive on culture for *Mycobacterium tuberculosis*, despite the absence of caseation necrosis in the tissue. Only six of the 19 patients with tuberculosis had significant reaction (9 mm or more) to PPD 5 U. Four patients with positive cultures for tuberculosis had positive reactions to Kveim test material. Of the 19 patients with tuberculosis 16 had positive scalene node biopsy results "compatible with sarcoidosis." Three patients had "noncaseating" granulomas in liver biopsy specimens, and all three had tuberculosis.

There were three instances of nontuberculous mycobacterial infection, two patients with metastatic breast carcinoma, one with histoplasmosis, one with hemosiderosis, one with berylliosis, and only three with sarcoidosis.

Open lung biopsy was the most effective diagnostic procedure in this study, establishing a definitive diagnosis in 53% of the patients.

This study should encourage us to continue close clinical observation on any patient in whom we diagnose sarcoidosis. In the diligent pursuit of a diagnosis, we should keep in mind that following primary or reactivation tuberculosis, tubercle bacilli may lie dormant in mediastinal lymph nodes for many years. Their presence on histologic specimens or on culture of such biopsy material may not be an indication of active tuberculous infection as the cause of the patient's current illness. Nor does positive clinical improvement during antituberculous therapy prove that such bacteriologic findings are the cause of the patient's illness. Spontaneous improvement may occur during the course of sarcoidosis, especially in patients with initial bilateral hilar adenopathy. Caution and skepticism should guide us in approaching the diagnosis of sarcoidosis.

John T. Flynn, MD (Associate Chief, Department of Medicine): To what extent do you think that the toxicity of antituberculous medication contributed to the deterioration of liver function in this patient?

Dr Woodburn: The patient's steady rise in serum alkaline phosphatase, transaminase levels, and bilirubin seemed more compatible with an obstructive pattern of jaundice. It was not clear, however, whether the hepatic granulomata were enlarging with secondary intrahepatic obstruction, or whether a drug reaction was also involved.

Harvey Salomon, MD (Attending Physician, Department of Medicine): Following the initiation of antituberculous chemotherapy, an increase in obstructive changes in the liver is characteristic of tuberculous involvement. There is swelling of tuberculous granulomas due to water absorption, as the tubercule bacilli are destroyed during the first few weeks of treatment. This has been demonstrated in children with tuberculous involvement of the liver.

Watchful waiting during the first months of antituberculous therapy has been advised, in the expectation of eventual improvement. Steroid therapy should be considered if improvement does not occur.

Satish Dhalla, MD (Attending Physician, Department of Medicine): The liver function tests are consistent with partial extrahepatic biliary obstruction or with intrahepatic granulomatous disease. Either tuberculosis or sarcoidosis, involving the lymph nodes at the porta hepatis, could cause extrahepatic biliary obstruction with an elevated serum alkaline phosphatase. The progressive impairment of liver function in this patient makes her a candidate for steroid treatment for the sarcoidosis, even though tuberculosis might also be present in the liver. She is presently receiving antituberculous treatment and that problem should be under control.

Dr Sharkey: Irrespective of the tuberculin test results, in treating a sarcoid patient with steroids, many pulmonary specialists will routinely initiate prophylaxis with INH at least, if not with two antituberculous drugs.

Dr Salomon: Do we know if this patient ever had a phase of sarcoidosis with hilar adenopathy?

Dr Woodburn: No, we do not.

Dr Sharkey: Tuberculosis is still common in this country. After a long decline at a rate of about 5% per

year, the frequency in the United States has recently risen slightly, possibly due to increased immigration from Southeast Asia.

Human beings are the only known reservoir of *Mycobacterium tuberculosis;* the spread is by means of aspiration of the infected droplets. After the initial infection, which is usually in childhood, the host develops a defensive lymph node reaction, but the organism may remain viable for many years inside body cells.

Ten years ago, INH prophylaxis was recommended for almost everyone with a positive tuberculin test and no prior treatment with INH; however, the hepatic toxicity of the drug has made us less enthusiastic in this regard at present. The importance of this toxicity has probably been overplayed, and we should discourage overconcern about it among our nonpulmonary colleagues. But we cannot be too cavalier about the problem either.

On this Medical Service, any patient with a productive cough and an abnormal chest radiograph must be suspected of tuberculosis. A prompt diagnosis will prevent unnecessary exposure of medical staff, nursing staff, other patients, and endoscopic instruments to the tubercle bacillus. Even when the sputum is scanty, careful examination of three satisfactory early morning specimens of sputum for acid-fast bacilli is necessary, particularly when the clinical picture and chest film are compatible with tuberculosis. The sputum may have to be secured with the aid of an aerosol to encourage deep breathing and cough. Proper acid-fast staining is essential. This careful search for acid-fast bacilli is more important than a computed tomographic scan, a chest consultant, or a bronchoscopy and lung biopsy.

A good isolation technique in the patient's hospital room does not require the staff to wear sterile gloves, gowns, and caps. A face mask on the patient effectively eliminates contagion, since the tubercle bacillus is spread only by air-borne droplets from coughing.

The patient we are discussing was unusual in that her sarcoidosis presented with granulomatous skin lesions and hepatic granulomata, without evidence of intrathoracic involvement. Many experienced physicians will hesitate to make a diagnosis of sarcoidosis unless intrathoracic granulomata are identified by biopsy of the pleura, a supraclavicular node, a mediastinal node, or the lung. When this patient recently developed cough, systemic symptoms, and marked changes on her chest radiograph, we initially suspected a severe reactivation of sarcoidosis with cystic pulmonary changes and possibly a fungus ball with *Aspergillus niger*. She had neither evidence of hilar adenopathy nor of pulmonary sarcoid involvement; however, her bone films were very convincing. No disease other than sarcoidosis, of which we are aware in this patient, could produce such skeletal changes. Furthermore, untreated systemic tuberculosis would be incompatible with this patient's benign clinical course in the several years since the hepatic and skin granulomas were first identified. Yet there is no question now that active pulmonary tuberculosis is present.

Isoniazid and rifampin are the preferred drugs for treating tuberculosis in this country; both are hepatotoxic but without cumulative toxicity when they are used in combination. With tuberculous hepatic involvement, most clinicians prefer to treat with INH and rifampin together since the combination is much more effective. Nevertheless, a serious problem arose in this patient with the marked increase in both the serum alkaline phosphatase level and the transaminase levels.

General guidelines for antituberculous treatment suggest that a rise in the serum transaminase levels to more than three times the normal range should prompt the physician to consider discontinuing the medication. Also, the appearance of hepatic symptoms and signs, with jaundice and an increasing serum alkaline phosphatase, is a generally sound indication to discontinue INH. Yet, such guidelines are not hard and fast rules. If the patient's preexisting liver disease were tuberculous, more INH rather than less would be indicated. That is why we recommended a repeat liver biopsy, which again indicated the presence of granulomas but no organisms. We cannot now determine whether such lesions indicate hepatic sarcoidosis, hepatic tuberculosis, or both. The earlier finding of hepatic granulomas suggests that sarcoidosis was and probably still is responsible.

In the absence of evident intrathoracic sarcoidosis, the patient's clinical picture was a most unusual one. At this time I would still be reluctant to treat her with steroids. My hope is that the liver disease will gradually improve, even though we continue treatment with INH and rifampin. The serum alkaline phosphatase level has decreased slightly, as have the serum transaminase levels. Hepatotoxicity caused by INH will often improve spontaneously despite continuance of the medication.

Such far advanced cavitary tuberculosis has a significant mortality and morbidity. If possible it would be wiser not to discontinue drug treatment. If the liver disease clearly was worsening because of the treatment, I would discontinue the INH and probably initiate ethambutol and streptomycin therapy. The reason for using only two drugs is because there is no solid evidence available indicating the superiority of three drugs over two in any disease caused by *Mycobacterium tuberculosis*, except with proven drug-resistant organisms. INH and rifampin are as good as, if not better than any other combination of drugs in the treatment of disease due to antibiotic-sensitive tubercle bacilli.

When antibiotic-resistant organisms are suspected, a third drug may be added. This applies especially to patients previously treated but currently in relapse, to patients from geographical areas known to be loci of resistant organisms, or to contacts intimately exposed to a patient with resistant organisms. Pyrazinamide is a good choice as the third drug, at least in New York City.

This patient still presents a significant problem. She has fever, has not yet regained much weight, and is still shedding tubercle bacilli in her sputum; however, she feels much better and her appetite has improved. At least her tuberculosis has not progressed. Commonly, patients with cavitary tuberculosis do not recover completely for many months despite effective treatment. They may be febrile and have positive sputum for long periods, but still show limited signs of improvement.

Contagion should not be of great concern at this point. Epidemiologic studies indicate that ten to 14 days of treatment with antibiotics largely prevents active contagion,

even though drug-sensitive acid-fast bacilli may still be identified in the sputum. While limitation of contagion may also occur with gross cavitary disease, in this situation we should be a bit more conservative in our precautions.

Deane Tseui, MD (Resident, Department of Medicine): In the case of a patient who after two weeks of antituberculous therapy is having a decrease in symptoms, would you move that patient out of isolation?

Dr Sharkey: Yes, except in the instance of gross cavitary disease. The bacteria that continue to be found in the sputum are probably not viable; I do not believe that it has ever been shown in such a situation that other persons have contracted the disease from a patient under active treatment.

Dr Dhalla: Was the liver biopsy specimen negative for acid-fast bacilli on culture?

Dr Sharkey: Yes.

Dr Lebowitz: What do you think is happening to her wrist?

Dr Sharkey: The fluid obtained on aspiration and the findings suggestive of uric acid crystals imply the presence of gout. I favor synovial biopsy in this patient because if the biopsy is positive for acid-fast bacilli, I would add at least one more antituberculous drug to her treatment.

What troubles me is that the joint lesions seemed to progress while she was on antituberculous treatment. If the biopsy specimens of the synovium were positive for granulomata but negative for acid-fast bacilli, I would assume the arthritis was due to sarcoidosis and would initiate steroid therapy, together with an additional antituberculous drug.

Samin Sharma, MD (Resident, Department of Medicine): What about the diagnostic and prognostic value of employing the angiotensin-converting enzyme (ACE) test in sarcoidosis?

Dr Sharkey: The impression is widespread that the ACE levels will be high during active sarcoidosis and will be low during remissions and the continued observation of its changes will help in predicting exacerbations.

However, there is little evidence to support those impressions, and the decision regarding steroid therapy should not be based on such changes alone. The ACE test is positive in many other conditions, and it may be negative in the patient with sarcoidosis; it is neither a very specific nor a very sensitive test.

Sarcoidosis is unpredictable, with a tendency toward spontaneous remission. Careful clinical evaluation is a better means of following the course of a patient with sarcoidosis.

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Spontaneous esophageal perforation: Boerhaave's syndrome

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Transmural spontaneous esophageal rupture was first described in 1724 by Boerhaave.[1] Before the report by Barrett in 1946,[2] this rare condition remained a pathologic curiosity being largely a post mortem diagnosis and almost always fatal. Many small series have been published subsequently describing the major clinical and pathologic features. A review of these reports, however, indicates that mortality remains unacceptably high. Reported mortality rates range up to 50%,[3,4] largely due to delayed diagnosis and inadequate management. The following report describes a patient with this condition and the various management options present in the literature, in an attempt to define those factors delaying diagnosis and to clarify the available range of treatment.

CASE REPORT

A 54-year-old man was admitted to the hospital because of persistent bilateral chest pain, epigastric pain, and fever of three days' duration following an episode of vomiting. The patient had a history of recent alcohol abuse; he was known to be a chronic alcohol abuser for many years.

On admission, the patient was found to be acutely ill with diaphoresis, dyspnea, and tachycardia. His temperature was 39.2 °C; pulse rate, 132 beats/min; respiration rate, 26/min; and blood pressure, 96/52 mm Hg. On examination of the chest, breath sounds were heard bilaterally with slight diminution of intensity at the left base. The abdomen was tender in the epigastrium, bowel sounds were hypoactive, and no masses were palpated. A chest roentgenogram showed blunting of the left costophrenic angle with a suggestion of fluid. No evidence of mediastinal or subcutaneous air was present. An electrocardiogram revealed sinus tachycardia of 130 beats/min and nonspecific ST-T changes.

FIGURE 1. Chest radiograph showing a left hydropneumothorax with cervical emphysema.

Laboratory values were as follows: hemoglobin, 16.5 g/dL; hematocrit, 46.3%; leukocyte count, 12,900/μL with 78% segmented forms, 3% band forms, 15% lymphocytes, and 3% monocytes. All other clinical laboratory tests were within normal limits.

A diagnosis of left-lower lobe pneumonia and pancreatitis was made. The patient was placed on broad-spectrum antibiotic treatment including tobramycin, clindamycin, and ampicillin intravenously. On the second day of admission, the patient became critically ill, septic, and severely dyspneic. A repeat chest roentgenogram (Fig 1) showed left-sided pneumothorax with an effusion. An intercostal chest tube was inserted resulting in symptomatic relief. Repeat radiography showed a decrease in the effusion but incomplete re-expansion of the lung.

Over the first 12-hour period following chest tube insertion, 2,700 mL of dark brown fluid drained from the chest. Culture of this fluid showed a growth of alpha-hemolytic streptococci. A diagnosis of esophageal perforation was suspected on the sixth day following admission and the patient was referred to the cardiothoracic surgery department. The diagnosis was confirmed by a Gastrografin swallow. The esophagogram (Fig 2) revealed extravasation of water-soluble contrast through a distal esophageal tear.

The patient was then transferred to the surgical service with an established esophageal fistula. On transfer he was stable; therefore a policy of continued conservative management was adopted. Two weeks after admission, because of the persistent fistula, the patient was scheduled for surgery and a total proximal esophageal diversion with end cervical esophagostomy combined with total distal esophageal occlusion was performed, utilizing a TA55 autosuture stapler. Regurgitation of gastric contents through the esophageal tear was minimized by gastrostomy decompression. A jejunostomy was also performed for nutritional purposes.

The patient had a satisfactory postoperative recovery and gradually became afebrile over the next two to three days. Prompt healing of the fistula occurred with adequate pleural drainage, antibiotics, and nutrition. The ingestion of an opaque meal on the 28th postoperative day did not reveal the presence of any esophageal leakage. The patient was taken to the operating room on the 34th postoperative day for closure of the cervical esophagostomy and the esophagogastrostomy employing the Collis gastroplasty to provide additional length with concomitant pyloroplasty as the definitive reconstructive procedure. This was done without difficulty and incident. The contrast study postoperatively showed complete patency of the distal esophagus with no evidence of leakage. The gastrostomy tube was removed several days later. On the 47th postoperative day the patient was discharged. He began eating a regular diet with no difficulty.

DISCUSSION

Postemetic spontaneous rupture of the esophagus is catastrophic and devastating and, in the majority of cases, results in the death of the patient. The diagnosis of esophageal perforation depends on suspicious awareness of the

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FIGURE 2. Esophagogram revealing extravasation of water-soluble contrast through distal esophageal tear.

possibility as well as on knowledge of the circumstances in which it may occur, the patient's symptoms, the presence of physical signs, and demonstration of the perforation and its secondary manifestations by radiography.

The delay in diagnosis of esophageal rupture may be attributed to various causes.[4] Alcoholics tend to present more than 12 hours after rupture and alternative diagnoses such as ruptured peptic ulcer, pancreatitis, or coronary thrombosis are made. Rupture frequently occurs in comatose or convulsing patients. There may be failure to appreciate the significance of the brownish color of the pleural fluid and the unusual organisms. The correct diagnosis was not made for six days in the case presented, despite cervical emphysema on the radiograph and the large volume of brown pleural fluid drained.

Although there is wide agreement that most perforations of the esophagus are best treated by immediate emergency surgical exploration, repair, and drainage, this is neither universally accepted nor always feasible. Of major concern are intrathoracic esophageal perforations diagnosed more than 18 to 24 hours after they occur, or those in which a fistula with acute suppuration is present. Delay of diagnosis and treatment beyond 18 hours appears to be a major factor contributing to morbidity and mortality. Recent reports of series of thoracic esophageal perforations mention mortality in excess of 60% with the usual surgical methods in late perforation, and between 10 to 30% with early treatment.[3,4]

The high mortality associated with late diagnosis and treatment of intrathoracic esophageal perforations has led to the development of several other methods of management, which are applicable under various circumstances. There has been great enthusiasm for reinforcing the suture repair of esophageal tears. Thal and Hatafuku[5] employed the gastric fundus as a reinforcing buttress patch; other researchers have used pedicles of the diaphragm,[6] pericardium,[7] intercostal muscle,[8] or latissimus dorsi, and of other muscles.[4] Variations on the esophageal exclusion described by Johnson and associates[9] include the partial exclusion and diversion techniques of Urschel and coworkers.[10]

In the case presented, the patient was transferred late to the surgical service with an established esophagopleural fistula six days after his original admission. Initially, conservative management including pleural drainage, intravenous hyperalimentation, and parenteral broad-spectrum antibiotics was adopted. Two weeks after admission, because of the persistent fistula, the patient underwent total proximal esophageal diversion. Prompt healing of the fistula occurred with continued conservative management. Reconstruction of the esophagus was accomplished at a later date. The single case reported here appears to indicate that this specific maneuver practically assures closure of the fistula and probable recovery of the patient in the treatment of a case of late distal esophageal perforation.

The esophagus heals poorly if there is inflammation and necrosis secondary to perforation. Continued contamination of the area and persistence of the esophageal leak after attempted repair have been a problem. This failure of esophageal healing and continued thoracic sepsis is associated with a high morbidity and mortality. It may be preferable to carry out initial surgical exclusion of the esophagus with diversion as described in the case presented and deal with reconstruction at a later date.

It is impossible to prescribe a technique applicable to all thoracic esophageal perforations. It is essential, however, to have a clear understanding of the clinical problems and the many techniques available for rational management of individual patients.

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See also pp 285–286.

The Mallory-Weiss syndrome

Case report and update on embolization versus intraarterial vasopressin results

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In 1929 Mallory and Weiss described the syndrome of upper gastrointestinal (UGI) hemorrhage due to mucosal lacerations in the region of the gastroesophageal junction in association with alcoholism.[1] The routine use of flexible fiberoptic endoscopy has demonstrated that these tears, previously thought to be uncommon, account for approximately 5 to 15% of cases of UGI hemorrhage.[2] They are also now known to be relatively benign lesions. Approximately 90% stop bleeding spontaneously with only conservative and supportive measures being required.[2,3] In those patients whose bleeding does not stop spontaneously, angiotherapy offers a relatively conservative and often successful alternative to surgery.[4] Such therapy is particularly useful in many of these patients who may be poor surgical candidates due to coexistent cirrhosis and coagulopathies.[2]

The following is a report of a case of Mallory-Weiss syndrome successfully treated by intraarterial infusion of vasopressin. A comparison of the success rates of the two major modes of angiotherapy (vasopressin infusion and embolization) for treatment of this syndrome is also presented.

CASE REPORT

A 33-year-old man was admitted to the hospital complaining of dizziness and copious vomiting of blood over the previous 12 hours. He had a long history of alcohol abuse and the previous evening had ingested approximately two pints of whiskey.

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Physical examination revealed a patient in mild distress with a blood pressure of 130/80 mm Hg; pulse, 80/min; respirations, 20/min; and a rectal temperature of 98.6°F. The patient denied any peptic ulcer disease or bleeding diathesis. The rectal examination was positive for blood. Endoscopy performed in the emergency room revealed bright red blood at the esophagogastric junction, but no tears were identified. Varices were not seen and the fundal mucosa was hyperemic. The pylorus and duodenal bulb were normal.

The patient was admitted to the intensive care unit and treated with intravenous cimetidine, antacids, nasogastric tube lavage (with iced saline and norepinephrine bitartrate), and blood transfusions. The patient received a total of seven transfusions of packed red blood cells and one transfusion of fresh frozen plasma over the next 24 hours without control of the bleeding. On admission his hemoglobin level was 13.9 g/dL and his hematocrit was 40%. Over the next 24 hours these values had dropped to 10.6 g/dL and 29.6%, respectively. Endoscopy at this time revealed an actively bleeding Mallory-Weiss tear at the esophagogastric junction. The patient was then referred to the radiology department for transcatheter therapy. A left gastric arteriogram revealed active extravasation in the distal esophagus (Fig 1). A vasopressin drip was started at 0.2 U/min and a repeat arteriogram at 30 minutes showed that the bleeding had stopped (Fig 2). The patient was continued on intraarterial vasopressin into the left gastric artery with tapering doses over the next 12 hours. A repeat arteriogram at that time showed complete control of the bleeding. The catheter was removed and no further bleeding occurred. Two days later a UGI series revealed a small hiatal hernia. The Mallory-Weiss tear was not visualized and there was no evidence of a gastric or duodenal ulcer. The patient was discharged in good condition and no further bleeding was reported.

DISCUSSION

Upper gastrointestinal hemorrhage secondary to a mucosal laceration at the gastroesophageal junction was first described by Quincke in 1879.[5] In 1929

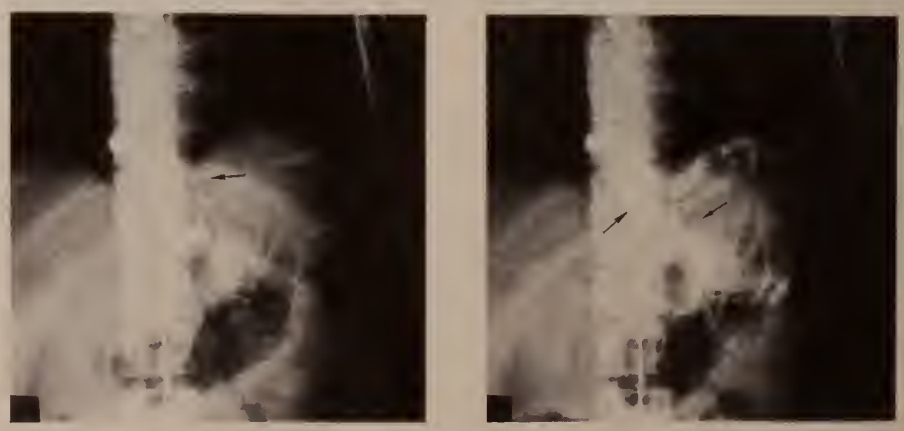

FIGURE 1. Selective left gastric arteriogram. Left, Beginning extravasation from esophageal branches of left gastric artery (arrow). Right, Extensive extravasation in the region of the esophagogastric junction (arrows).

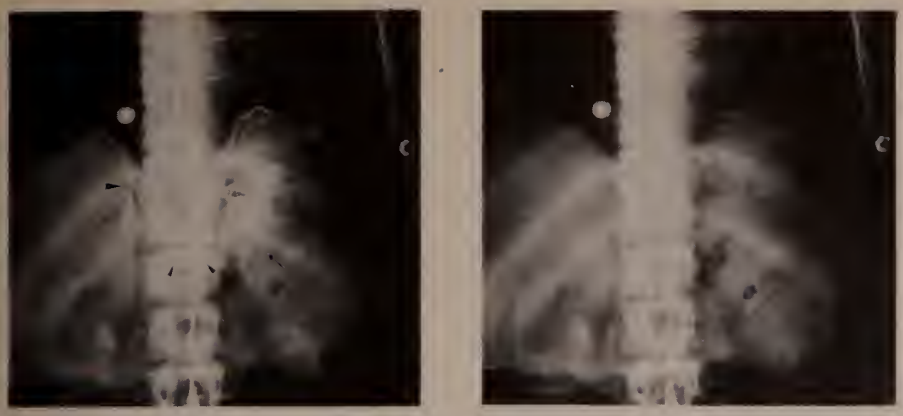

FIGURE 2. Post-pitressin left gastric arteriogram. Left, Diffuse vasoconstriction of peripheral branches of left gastric artery with no evidence of extravasation (arrows). Reflux is seen bilaterally into the inferior phrenic arteries, (small arrowheads), and into the superior adrenal artery (large arrowhead). Right, Late venous phase showing no accumulation of contrast in the esophagus or stomach.

Mallory and Weiss described this lesion in association with the "persistent nausea, retching, and vomiting of a long and intense alcoholic debauch." [1] Numerous etiologies are now known to produce similar tears including other causes of retching and vomiting (eg, travel sickness, uremia, migraine, pancreatitis, endoscopy, and chemotherapy), straining at stool, childbirth, heavy lifting, hiccupping, coughing, seizures, blunt abdominal trauma, and cardiopulmonary resuscitation.[2,6-8]

The common pathogenesis of UGI hemorrhage appears to be the development of high, transient transmural pressure gradients between the intragastric pressure and the intrathoracic pressure at the gastroesophageal junction.[2,3,7,9] Such an unacceptably high pressure gradient may lacerate the mucosa at this junction, resulting in the UGI hemorrhage known as the Mallory-Weiss syndrome. It may also cause complete perforation in the same area, resulting in the Boerhaave syndrome. Although these entities share a common pathogenesis, their clinical evolution and expected outcome are significantly different.[9]

Prior to the development of the flexible fiberoptic endoscope, Mallory-Weiss tears were thought to be uncommon lesions. They are now known to account for approximately 5 to 15% of cases of UGI hemorrhage.[2] A high index of suspicion followed by careful endoscopy are necessary for diagnosis. Barium or Gastrografin studies are of limited value in the direct diagnosis of a Mallory-Weiss tear, although they may demonstrate other potential sources of bleeding or the presence of a hiatal hernia, which is a common feature of this syndrome.

Since approximately 90% of bleeding due to Mallory-Weiss tears stop spontaneously, initial management should be conservative, consisting of iced saline lavage, antiemetics, antacids, intravenous or oral cimetidine, and, if necessary, blood transfusions.[3] If these measures are unsuccessful, the intravenous administration of vasopressin may result in a cessation of bleeding. However, its systemic effects, which are discussed below, may limit its application.[3,10]

Although surgery is frequently the next step for continued bleeding, angiotherapy offers a more conservative alternative.[4,11] Such radiologic procedures consist of either infusion of vasopressin selectively into the celiac axis or subselectively into the left gastric artery, or embolization of the left gastric artery, both performed through a percutaneously placed angiographic catheter. Angiotherapy has potential complications that must be considered before it is initiated. Vasopressin, whether administered intravenously or intraarterially, has both hormonal and cardiovascular effects. The antidiuretic properties of vasopressin are well known and the problems may be handled medically during vasopressin infusion. The more difficult problems are those related to the direct effects of vasopressin on the heart and to systemic hemodynamic effects. Among the complications observed are the following: decrease in coronary blood flow and cardiac output; decrease in arterial P_{O_2}; arrhythmia; acute cardiac failure; cardiac arrest; acute myocardial infarction; acute pulmonary edema; hypertension; decrease in splanchnic flow with portal and mesenteric vein occlusion; and reversible ischemic colitis.[7,12] Locally infused vasopressin has precipitated left gastric artery and mesenteric artery occlusions secondary to thrombosis.[7]

Complications related to embolotherapy are due to acute cessation of blood flow to the organ supplied. If adequate collateral circulation is present, the organ can generally survive the acute ischemic episode. In the face, however, of prior surgery, which may have obliterated potential collaterals, or diffuse atherosclerosis, adequate collateral flow may not be available thereby leading to irreversible tissue ischemia and infarction.[6] Regurgitant embolic material is another hazard leading to visceral or peripheral extremity emboli. With the potential complications in mind, it is obvious that the approach to each patient must be individualized. If no overriding contraindication is present to the use of either modality, a review of the success rates would appear to be a logical step in determining which method to employ in a given situation.

In 1980 Fisher and associates[4] reviewed the literature and found that a total of 16 cases of Mallory-Weiss tears treated with intraarterial vasopressin had been reported; they added 13 cases of their own. The researchers also found 14 previous cases of embolization for Mallory-Weiss tears and added two cases of their own.[4] Rahn and colleagues reported two cases of intraarterial vasopressin and two cases of embolization for Mallory-Weiss tears.[13] Including the case reported in this paper, there have been 32 cases of intraarterial vasopressin and 18 cases of embolotherapy for Mallory-Weiss tears reported in the English language literature to date. The success rate in each group was 72%, which would suggest that no statistical difference existed. However, many of the vasopressin failures occurred when this vasoconstrictor was infused into the celiac axis and not subselectively into the left gastric artery. In celiac axis infusions the tip of the catheter may be beyond the origin of the left gastric artery, which is the major artery involved in Mallory-Weiss tears. Since all embolizations must be done subselectively into the left gastric artery, a comparison of results from subselective catheterizations would appear more valid. Of the 32 patients treated with intraarterial vasopressin, 19 were infused into the celiac axis and 13 subselectively into the left gastric artery. The success rate for permanent hemostasis in the celiac axis group was 64% (12/19), while that in the subse-

lective left gastric artery group was 92% (12/13). This latter success rate is significantly greater than the 72% (13/18) achieved in embolization of the left gastric artery. Thus, if subselective catheterization of the left gastric artery is achieved, vasopressin infusion should be the treatment of choice unless specific contraindications to its use exist. If vasopressin infusion fails, embolization therapy may then be attempted once vasoconstriction has subsided and the threat of regurgitant emboli has diminished.

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See also pp 285–286.

Spontaneous rupture of the liver during pregnancy

A case report and review of the literature

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Spontaneous rupture of the liver is a rare, life-threatening complication of pre-eclampsia or eclampsia. First reported by Abercrombie in 1844, approximately 130 cases have been published, most of these in the obstetrical literature.[1] Although long recognized as a clinical entity, the pathogenesis of this disorder remains obscure. While disseminated intravascular coagulation (DIC) has often been suggested as a precipitating factor in liver rupture, the following case does not lend support to this theory.

Case Report

A 39-year-old woman, para 1021, gravida 4, in her 41st week of gestation was admitted to the hospital with a complaint of severe right upper quadrant pain of six hours duration. During the week prior to admission the patient had experienced increasing headache and blurring of vision.

On admission her blood pressure was 130/80 mm Hg; pulse, 88/min; and respirations, 20/min. Chest and cardiac examinations were normal while abdominal examination showed a distended (pregnant) abdomen with moderate right upper quadrant tenderness and guarding, without rebound tenderness. The patient had moderate (2+) pedal edema; hyperreflexia (3+) was present. Laboratory data revealed a WBC count of 13,400 with a normal differential; hematocrit, 41.9%; platelets, 146,000; prothrombin (PT) and partial thromboplastin times (PTT) of 12.6 and 41.5 seconds with controls of 12.6 and 34.4 seconds, respectively; and a fibrinogen level of 468 mg/dL. Urine analysis showed 2+ proteinuria. When the fetal heart rate precipitously dropped to 80/min, the patient was taken for a cesarean section with the diagnosis of fetal bradycardia and possible uterine rupture.

A midline abdominal incision was made and a low transverse cesarean section was carried out, delivering a 2.1 kg male child with Apgar scores of 5 and 8 at one and five minutes, respectively. After closure of the uterus, active bleeding was noted to be coming from the right upper quadrant. The incision was extended upwards and a laparotomy showed the liver to have many lacerations and profuse blood flowing from the anterior portion of the right lobe all the way to the lateral aspect of the liver. Packing with purified bovine microfibrillar collagen and oxidized regenerated cellulose afforded some hemostasis. Intraoperatively the patient received five units of packed red blood cells and two units of fresh frozen plasma. The incision was then closed, with a Jackson-Pratt drain remaining in the right upper quadrant.

Over the next three hours the patient lost approximately 1L of bright red blood through the abdominal drain. Her hematocrit was 25.4%; platelets, 40,000; fibrinogen was too low to count; and PT and PTT were greater than twice the controls. She received three units of packed red blood cells, two units of fresh frozen plasma, and ten units of

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platelets. The patient was again brought to the operating room because of intraperitoneal bleeding. Upon incision, 1,500 cc of blood was drained and there was gross bleeding from many decapsulated areas of the right lobe. The left lobe was pale and mottled, and was boggy to palpation. The liver would not hold sutures, and collagen and cellulose afforded little hemostasis. Finally, two gauze rolls were pressed against the liver and tied together, controlling the bleeding. The patient received one unit packed red blood cells and four units of platelets intraoperatively. The patient continued to require blood products, receiving a total of five units of packed red blood cells, four units of fresh frozen plasma, and 11 units of platelets.

Clotting parameters returned to normal, and three days later the gauze packing was removed during laparotomy. At that time the liver appeared less edematous with clotted blood covering the decapsulated areas. During the next two weeks the patient did well but experienced a right-sided hemothorax requiring placement of a chest tube for adequate drainage. In addition, the patient continued to complain of mild to moderate right upper quadrant discomfort. A computed tomographic (CT) scan revealed coagulated blood forming a right subphrenic hematoma. This was drained percutaneously with irrigation three times a day. The patient was discharged from the hospital 32 days after admission.

Discussion

Although a rare entity, the clinical features of spontaneous liver rupture during pregnancy are such that Severino and associates were able to construct a composite history summarizing these features: a multigravida; in her 30s; in her last trimester; and with hypertension, proteinuria, and abdominal pain.[2] Both Henny and colleagues[3] and Bis and co-workers[4] confirmed this characterization, finding that 82% of their patients had more than one child, had an average age of 31.7 years, and more than 80% were in their last trimester. Despite this stereotypical presentation, the diagnosis of spontaneous liver rupture is usually not made preoperatively, as in this case.

The most common cause of liver rupture in general is trauma, but the mechanism of rupture during pregnancy is unknown. As early as 1906, Devic and Beriel suggested that, "In traumatic rupture, the rupture is the cause of the hemorrhage. In spontaneous rupture, the hemorrhage is the cause of the rupture. The chain of events leading to the rupture are infarction, hypervascularization of the periphery, rupture of a vessel, intrahepatic hemorrhage, with resulting rupture of the tissue and production of a subcapsular hematoma . . . ." [5]

Speert and Tillman[6] noted that patients with eclampsia are notorious for their hemorrhagic tendencies, and that cerebral, rectus muscle, retroperitoneal, and splenic hemorrhages have been found in such patients. These researchers also suggested that degenerative changes in connective tissues may also play a role in liver rupture.[6]

Many investigators have maintained that rupture of the liver in pregnancy is caused by minor trauma to an already susceptible organ. Indeed, Abercrombie's case is that of a woman who tied her handkerchief around her waist to relieve her gastrodynia.[1]

Other investigators have defined a unique group of preeclamptic/eclamptic patients with hemolysis, elevated liver enzymes, and a low platelet count presenting with right upper quadrant pain.[7] The patient reported here did not manifest the hyperbilirubinemia nor the abnormal peripheral blood smear of these patients.

Finally, intraoperative and post mortem biopsy specimens of the liver often demonstrate fibrin, suggesting that disseminated intravascular coagulation (DIC) during preeclampsia or eclampsia might lead to hemorrhage and subsequent rupture. Mokotoff and associates[8] stated that infarction will occur in DIC only if active mechanisms of fibrin clearance are blocked. He proposed that the reticuloendothelial system is desensitized by prior pregnancy and prevented from clearing fibrin. This might explain why liver rupture occurs primarily in the multigravida while primagravidas have a higher incidence of preeclampsia and eclampsia.[8] However, the cause of the liver rupture in the patient described earlier did not apper related to DIC. She had a normal coagulation profile prior to surgery and no clinical evidence for DIC at the time of surgery when the liver rupture was noted. The DIC, characterized by a low platelet count, low fibrinogen, and elevated PT and PTT, occurred, only after surgery and may have been related to the cesarean section or liver rupture itself. While DIC may have contributed to the hemorrhage, there is no evidence that it actually initiated the bleeding. We could find no other case in the reported literature that so clearly argues against DIC as an initiating factor in liver hemorrhage and rupture. The cause of this patient's hemorrhage and rupture remains unknown.

Once the diagnosis of liver rupture has been made immediate steps to control the hemorrhage must be taken. Conservative, nonsurgical management resulted in maternal mortality in 96% of the patients reviewed by Henny and colleagues, whereas surgical therapy yielded an overall mortality of 33%.[3]

Goodlin and co-workers described two cases of liver rupture and suggested ultrasonic computerized tomographic monitoring in cases of subcapsular hematoma without frank rupture.[9]

After the bleeding site is located, hemostasis must be established. This may be achieved by compression, suture, gauze packing, topical agents, arterial embolization, omental pedicles, or hepatic artery ligation.[10] The pregnancy should be terminated at laparotomy for several reasons: 1) to avoid labor with its increased intraabdominal pressure; 2) to treat the preeclampsia, since the liver rupture may be a complication either of preeclampsia or true eclampsia; and 3) to avoid maternal effects on fetal survival, since viability is greater if the infant is delivered.[2]

Adequate drainage of the hepatic bed postoperatively is important to avoid diaphragmatic irritation and persistent subphrenic hematoma, as was performed in our case. Cardiopulmonary status should be monitored carefully, as pleural effusion is not an uncommon finding.[10,11] The cause of the postoperative hemothorax in our patient is uncertain.

In summary, preoperative diagnosis of liver rupture during pregnancy is rare despite a characteristic presentation in pregnant multiparas with preeclampsia or eclampsia. The cause of this spontaneous rupture is unknown, although DIC and unsuspected trauma are thought to play a role. In the present case, DIC was clearly shown not to be an initiating factor.

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See also pp 286–288.

Unusual presentation of a giant leiomyoblastoma of the stomach

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Tumors of the smooth muscle tissue are the most common nonepithelial tumors of the stomach. They are usually small in size, asymptomatic, and often undiagnosed during life. Clinically, leiomyomas represent about 40% of all benign gastric neoplasms, and leiomyosarcomas represent about 25% of all gastric sarcomas.[1]

In 1960, Martin and co-workers[2] described for the first time an uncommon type of gastric tumor derived from the smooth muscle tissue, with the same macroscopic features as the leiomyoma, but with completely different histologic features. These tumors have been given several names such as myoid tumors, bizarre leiomyomas, epithelioid leiomyomas, etc.[3,5] However, in the recent classification of the World Health Organization (WHO, 1977) they are identified as leiomyoblastomas.

We recently observed a case of this uncommon tumor, presenting as a giant exogastric mass in a patient with an interesting previous history.

CASE REPORT

A 50-year-old man was admitted to the hospital for an abdominal mass that had appeared about one month before. His past history included hospitalization for a right bundle-branch heart block, and an operation for drainage of a suppurative cyst of the gastrocolic ligament.

Physical examination at the time of admission revealed a large rounded painless centra-abdominal mass of soft elastic consistency and with a slightly irregular surface. Radiograph of the chest was normal. An ECG revealed right bundle-branch heart block, with supraventricular extrasystoles.

FIGURE 1. Barium enema examination showing the displacement of the transverse colon by an extrinsic compression.

A barium enema examination revealed a large rounded mass that compressed and displaced the intestinal loops, the transverse colon, and right colonic flexure (Fig 1). Radiographic studies of the stomach were unremarkable (Fig 2). An abdominal sonogram showed a large solid mass with colliquative areas separate from the liver and without any connection to great abdominal vessels. A computed tomographic (CT) scan of the abdomen confirmed the presence of a voluminous solid and vascularized growth in the mesogastrium, with normal findings of the liver, pancreas, kidneys, adrenal glands, and lymph nodes. Selective arteriography of the celiac axis and the superior mesenteric artery revealed a large mass approximately 16 cm in diameter vascularized by neoformed vessels from gastroduodenal and gastroepiploic arteries and situated in the center of the abdomen (Fig 3).

The patient underwent an exploratory laparotomy with the preoperative diagnosis of intraabdominal mass of an undetermined nature. At surgery a large encapsulated,

FIGURE 2. Radiographic study of the stomach showing normal findings.

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FIGURE 3. Selective arteriography of the hepatic artery showing a large abdominal mass vascularized by new vessels from the gastroepiploic arc.

bosselated, dark red mass of soft elastic consistency was found. The mass extended into the gastrocolic ligament from the greater gastric curvature to the transverse mesocolon. It was carefully isolated, and the gastroepiploic arc delimiting the mass inferiorly was tied and sectioned. The connection with the great curvature of the stomach was reached (Fig 4). The mass was removed with a 3-cm wedge of the stomach. Careful inspection revealed no metastases.

On gross examination, the tumor was found to be a large encapsulated dark red mass, measuring 20 × 16 × 3 cm. The cut surface was tan-white and white-greyish in color, with large areas of cystic degeneration and hemorrhage. On microscopic examination, the tumor demonstrated hemorrhagic areas delimiting groups of polygonal cells, with eosinophilic cytoplasm and irregular nuclei. Numerous giant multinucleated cells were found. Other areas of spindle cells, with clear cytoplasm, dispersed in interlacing bundles were present. Rare mitoses were seen (less than one per high power field). This tissue extended into the gastric wall as far as the muscolaris mucosae. The mucosa of the resected stomach presented a pattern of superficial gastritis. The final histologic diagnosis was gastric leiomyoblastoma (epithelioid leiomyoma) (Fig 5).

The postoperative course was uneventful, and the patient was discharged on the tenth postoperative day. The patient has been well after 16 months.

Discussion

In early stages leiomyoblastomas are intramural, but may later extend into the gastric cavity as a submucosal mass

FIGURE 4. Intraoperative view showing the connection of the large mass with the greater curvature of the stomach.

(endogastric growth),[1] or into the peritoneal cavity as an exogastric formation,[6] as occurred in the patient described earlier. In rare instances they may have an hour-glass aspect. The surface may be smooth or lobulated; there may also be areas of necrosis, cavitation, and hemorrhage. These tumors can communicate with the gastric cavity or break into the peritoneal cavity.[7] Suppuration is also possible, with the tumor evolving into an abscess either in the gastric wall or in the peritoneum, as similarly described for intestinal leiomyomas. This uncommon evolution probably occurred in our patient seven years earlier, when he underwent an operation with a generic diagnosis of suppurative cyst of the gastrocolic ligament that was treated with external drainage. Probably, even then, the pedicle of communication with the gastric wall was very small or, at least the connection of the mass with the stomach was not found.

One third of all cases of leiomyoblastoma are asymptomatic.[5] The principal manifestations are epigastric pain, nausea, vomiting, weight loss, gastrointestinal hemorrhage, and palpable mass. In our patient the only manifestation was an epi-mesogastric palpable and movable mass, without any evidence of gastrointestinal disease.

The most important diagnostic procedure for leiomyoblastoma is the radiographic examination, which in about 80% of cases clearly reveals a filling defect in the stomach.[1,5] Other diagnostic tools are gastroscopy, laparoscopy, or CT scan, and selective arteriography. In our patient all of the diagnostic tests were performed, including abdominal sonography and selective arteriography of the celiac axis and superior mesenteric artery.

Leiomyoblastomas are not encapsulated, and therefore the peripheric tumor cells may be mixed with the cells of the surrounding gastric wall. This characteristic may cause confusion in distinguishing benign from malignant forms.

The histology of leiomyoblastomas may be varied and bizarre. The structure is composed of spindle-shaped cells, rounded and polygonal rather than oblong, and giant epithelioid cells with abundant clear cytoplasm surrounding the excentric nucleus. The cells are often surrounded by a framework of reticulum fibers. As previously stated, the term leiomyoblastoma makes a distinction between epithelioid leiomyomas and leiomyosarcomas

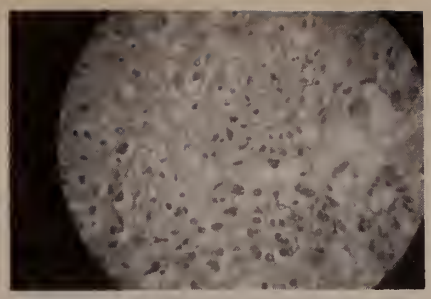

FIGURE 5. Microphotograph of the gastric leiomyoblastoma (epithelioid leiomyoma) showing numerous giant epithelioid cells and spindle-shaped cells. (Hematoxylin and eosin stain; original magnification × 400.)

according to a benign or malignant character as revealed by histologic examination. The benign or malignant character of this type of tumor is not completely clear, and on occasion an error in classification may be made (in fact, metastases have been found in tumors considered histologically benign). Therefore, some researchers[1,4] consider the observation of two or more mitotic figures per 50 high-power fields a criterion of malignancy. Other authors,[5,8,9] however, verifying the inconstancy of this observation regarding the evolution of these tumors, have stated that the number of mitoses is insufficient as a single criterion, and the term malignant leiomyoblastoma is preferred to that of leiomyosarcoma. It follows that the only evidence of malignancy is the presence of metastases or invasive intra- or extragastric growth that may be found during actual or subsequent surgery. Therefore, every smooth muscle tumor of the stomach must be suspected of malignancy until time and evolution prove the contrary. Additional criteria of malignancy of the epithelioid leiomyoma would be the macroscopic tumor size (larger than 6 cm), the localization in the posterior wall of the stomach and at the level of the fundus, the small size of the cells, the absence of reticulum fibers, and an alveolar arrangement of the tumor cells.[4,5,9]

The surgical procedure recommended in the treatment of gastric leiomyoblastomas varies from enucleation of the tumor to total gastrectomy.[10-12] In our opinion, the procedure of choice consists of a wide local excision (tumor with 2 to 3 cm of surrounding gastric wall), since simple enucleation may be inadequate. The situations in which partial or total gastrectomy are indicated are the following: histologic diagnosis of malignancy (at frozen section or at definitive examination); voluminous neoplasm involving the main part of the

stomach; and many localizations or recurrences.

There has been no correlation to date between survival and surgical procedure,[5] and for this reason we think that the least extensive resection by which the entire tumor may be removed is sufficient. The standard regional lymphadenectomy appears to be superfluous. The effect of radiotherapy and treatment by cytostatic agents (Actinomycin D) has not yet been established.[12]

In conclusion, we think that apart from the unusual presentation of some tumors, controversy still exists about the biologic behavior of gastric leiomyoblastoma. In our opinion, the best approach to define the benign or malignant nature of this type of tumor is to utilize all the available criteria, including clinical symptomatology, localization of the tumor in the gastric wall, tumor size, the presence or absence of mucosal infiltration, the number of mitotic figures, and, most importantly, the findings on histologic examination.

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Fibrosarcoma following radiation therapy for breast carcinoma

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Sarcoma following irradiation is a rare but well-described entity following the report by Perthes in 1904.[1] Osteogenic sarcoma and fibrosarcoma are the most frequently described types, although various other sarcomas have been reported.[3–12] Soft tissue sarcoma developing after radiation therapy for carcinoma of the breast is rare and usually fatal.[10] Only eleven cases of fibrosarcoma reported in the literature have been found to be associated with radiotherapy given for breast cancer. These cases are discussed and reviewed by O'Neill and associates,[10] Friedman and colleagues,[11] and Ferguson and co-workers.[12] The following report is of a patient who developed extraskeletal fibrosarcoma 25 years post irradiation for breast cancer.

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Case Report

A 61-year-old woman underwent a biopsy of a right supraclavicular mass in September 1979 that revealed a fibrosarcoma. A right radical mastectomy had been performed 25 years prior to this admission for breast carcinoma followed by radiation therapy to the chest wall and supraclavicular region with a total dose of 3000 rad. One year later, the patient underwent a left simple mastectomy. The patient remained well until 17 years later when she developed pain in the right elbow that recurred intermittently without evidence of a mass. However, nine months prior to this admission her right arm pain worsened and a mass appeared in the right supraclavicular fossa.

The patient then received 6,200 rad of external irradiation to the mass, followed by an Iridium-192 implant with no shrinkage of the tumor and no improvement of her symptoms. Six months later the patient developed low back pain and lower extremity weakness, numbness, and pain. A chest radiograph revealed many nodules consistent with pulmonary metastases. A computed tomographic (CT) scan confirmed spinal but not brain metastases. Steroids and radiation therapy to the brain and thoracic spine were given with modest reduction in pain but no improvement of lower extremity weakness. Chemotherapy with vincristine, adriamycin, and CCNU was instituted. However, the patient developed pneumonia and died on July 22, 1980.

At autopsy, a sarcoma composed of interlacing bundles, some with herringbone pattern and spindle-shaped cells with elongated nuclei, was found invading the axillary nerve and subclavian artery. Examination of a section from a right lower lobe nodule revealed a focus of similar sarcoma. Sections of cerebrum, cerebellum, and brain stem were negative but a tumor nodule enmeshed in the

nerve roots of the lower thoracic spine was found.

Discussion

Cahan and associates[2] suggested the following criteria for a sarcoma to be considered radiation-induced: (1) The sarcoma should arise in the area subjected to the irradiation. (2) A latent period (in years) must exist between the time of irradiation and the development of the sarcoma. (3) The sarcoma must be diagnosed on histologic examination.

Hardey and colleagues[3] thought that since there is no associated correlation between the dose of radiation and the incidence of sarcoma, it is preferable to use the term "post-irradiation sarcoma" instead of radiation-induced sarcoma, indicating merely the chronologic events of irradiation and the detection of sarcoma. In the case reported here, the sarcoma arose approximately 25 years after irradiation. The average latent period reported previously is 10.2 years. Also, patients who developed post-irradiation sarcoma received from 3,300 rad to 10,000 rad.[9] Our patient had received 3,000 rad orthovoltage radiation to the right supraclavicular region. In most reported cases the treatment included radical surgery or radiation therapy and the survival ranged from three to 24 months.[6,9,10] Several long-term survivals have been reported after radical surgery.[12] Our patient died nine months after the diagnosis of sarcoma was made.

As the survival rate of breast cancer improves with the application of improved modalities of treatment as, for example, adjuvant chemotherapy, it is possible that there will be an increasing number of patients with masses in or near an irradiated site. Radiation therapy is increasingly being utilized as the primary modality of treatment after lumpectomy for early stage breast cancer. It would seem, therefore, that the population at risk for post-irradiation sarcoma will be increasing in the future. It must be emphasized that histologic confirmation should be obtained before instituting therapy for recurrent breast cancer. If fibrous proliferation is found, an aggressive surgical resection of the irradiated area may be the treatment of choice.[11] None of the reported patients including our own had evidence of recurrent breast cancer.[10]

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RUPTURE OF THE ESOPHAGUS BY EMESIS

Most cases of rupture of the esophagus associated with vomiting have been reported under the title of spontaneous rupture of the esophagus. I favor referring to the condition as rupture of the esophagus by emesis since it points to the significant etiologic factor. Although there has been much discussion in the literature as to whether many of these cases have pre-existing esophagitis or peptic ulcer of the esophagus, it should be emphasized that clinically there is usually no history definitely pointing to such previous esophageal disease, and in the cases submitted to early operation conclusive evidence of pre-existing ulceration is usually lacking.

In many patients with rupture of the esophagus by emesis an erroneous diagnosis of perforated ulcer is made and an upper abdominal exploration performed. Unless the correct diagnosis is made early and immediate thoracotomy with closure of the perforation is carried out, the patient rarely survives.

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(*NY State J Med* 1955; 55:1626)

This section is designed to offer rapid publication (usually within 1–3 months) of new clinical, epidemiologic, and laboratory observations, as well as of comments on articles published in the Journal *or on any topic related to the role of the physician. Letters should be typed double-spaced and should include the professional affiliation, highest academic degree, address, and signature of each author. Preference is given to letters not exceeding 450 words. All letters are personally reviewed and acknowledged by the Editor. Address correspondence to Editor,* New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042.*

Alprazolam-induced manic reaction

TO THE EDITOR: Tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) have been documented to induce mania or hypomania, especially in bipolar patients.[1,2,6-8] While the value of benzodiazepines for the treatment of depressive disorders has not been established, alprazolam, a triazolobenzodiazepine, has been reported to be effective in the treatment of depression.[3] Recently, the induction of mania by alprazolam was reported by some authors.[4,5] We report here a similar case.

Case Report. A 54-year-old woman presented with a complaint of depression and agoraphobia with panic attacks for the past ten years. Because of the latter, the patient had not ridden buses or subways for five years, and had been unable to leave her home for one month at a time. The course of her illness was punctuated by periods of excessive energy during which she stayed up all night, moved furniture about, and experienced racing thoughts. The patient's depression worsened 1½ years earlier following the death of her husband.

On admission her symptoms included insomnia, lack of appetite during the day, excessive eating at night, some weight loss, anhedonia, dysphoric mood, agitation, crying spells, impaired concentration, multiple somatic complaints, and seriously impaired functioning. The patient had feelings of hopelessness and guilt, and she experienced difficulty in making decisions.

Her panic component was manifested by psychic anxiety, finger-wringing, severe itching, a choking sensation, fear of dying, feeling that she was dead or that she might explode, "like I am going to jump out of my skin," and an inability to use the elevator.

The patient had been treated with many TCAs in the past, and all were discontinued because of side effects. In the hospital, a four-week trial of oxazepam 15 mg orally three times a day produced some remission of generalized anxiety. However, the depressive and panic clusters remained unaltered. The medication was changed to alprazolam, which was slowly increased over a four-week period from 0.25 mg/d up to 2 mg/d in divided doses. The patient's depression and panic attacks abated; most noticeably, she was once again able to ride buses and trains while on passes from the inpatient unit. She underwent surgery for hernia repair and returned to the unit without difficulties.

However, after three days on alprazolam 2 mg/d, the patient began experiencing irritable moods, racing thoughts, pressured speech, less need for sleep, and a sense of increased levels of energy. She was cleaning incessantly on the unit, and felt that everything was moving very quickly around her. These changes were noticeable to staff, patient, and family alike. The total daily dose of alprazolam was decreased over a two-week period, but had to be discontinued due to persistent hypomanic symptoms. With the discontinuation of alprazolam, the hypomanic symptoms improved but the panic attacks became severe. Therefore, four days later alprazolam was reinstated at a reduced dose of 1.25 mg/d.

Nevertheless, over the following three days the patient became hypomanic. However, her panic disorder once again improved. At this point, lithium carbonate 300 mg orally three times a day was added to the treatment, with excellent results. The patient's mood stabilized within one week on a lithium level of 0.60 mEq/L. The panic disorder continued in remission. The patient was discharged from the hospital one week after the combined drug treatment had been started. She remained fairly stable three months later.

Discussion. Tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs)[1,2,6-8] have been extensively reported to induce mania or a hypomanic state in patients with major affective disorders. Even trazodone, a triazolopyridine derivative with antidepressant activity, chemically unrelated to other antidepressants, has been reported to induce mania in depressed patients.[9]

Nonetheless, this report and those published previously[4,5] show that despite alprazolam's unique chemical structure it, too, may induce mania in depressed patients. The patient described here did have some of the risk factors involved in drug-induced mania in depressed subjects. These include being female and having a history of bipolar cycles.[8,10] This patient also illustrates that if reduction in dose, or discontinuation of the drug, is not followed by complete remission of manic symptoms, the use of lithium salts may be indicated. Our patient responded to a relatively low lithium level (0.60 mEq/L). Lower lithium dose/blood level ratios are associated with older age, being female, and lower sodium intake.[10]

This report should serve to caution physicians to monitor carefully patients taking alprazolam, especially if they have a history of mania or hypomania.

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Appendiceal diverticulitis

TO THE EDITOR: It is no coincidence that there is a dirth of American literature describing certain conditions of the appendix such as appendiceal diverticulitis and chronic appendicitis. The world literature is replete with references to both of these conditions; we suggest that there may be a relationship between them.

Chronic appendicitis as a specific disease entity has been a topic of controversy for many decades. However, there is no doubt that patients may develop classical signs of acute appendicitis that may subside and appendices removed after several of these attacks often show destruction of the muscular layer with replacement fibrosis. The following presentations of chronic appendicitis should be considered: (1) recurrent acute attacks; (2) chronic pain with intermittent exacerbations; (3) persistent grumbling and crampy pain in the right iliac fossa without acute attacks.

As described in our article published in the *Journal* (1986; 86:155–156), appendiceal diverticulitis may persist with an indolent course or repeated acute attacks, suggestive of chronic appendicitis. We propose that the only way to determine if the appendix may be responsible for more chronic symptoms is to do a multi-institutional study. All patients undergoing incidental or therapeutic appendectomy would be screened for a history of right lower quadrant symptoms prior to the acute illness and surgery. Each appendix removed would be carefully examined for diverticula and evidence of prior inflammation. Then, with a significant number of patients and specimens, a correlation—if one exists—may be identified. Only a study performed in this manner will ultimately answer the question: "Appendiceal Diverticulitis and Chronic Appendicitis: Is There A Relationship?"

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Micropsia: Lilliput revisited

TO THE EDITOR: The essential feature of psychogenic micropsia is that people and objects appear to be far away, often described by viewers as if they were "looking through the wrong end of a telescope." It may occasionally occur in visual imagery with the eyes closed, but it most often occurs with the eyes open. I previously reported that the basic dynamics involved in patients with micropsia is a feeling of separation from people and the environment in an effort to control anxiety, a sense of weakness, and insecurity that is either transitory or a general feature of personality functioning.[1] Individual cases have been described by Inman,[2] Bartemeier,[3] and Lewy,[4] and observations have also been made by Fenichel.[5] The psychodynamics of micropsia and comments on published cases and observations have already been reported.[1] I have also encountered several descriptions of micropsia in recent fiction. Two works depict scenes viewed directly with the eyes open, and a third involves a visual imagery setting.

In *Summer of the Red Wolf* by Morris L. West,[6] the protagonist writer returns to the home of his physician friend in the north of Scotland after a series of turbulent events. "My homecoming . . . was strange . . . Suddenly everything was small: the houses like toy-town cottages, the fields like pocket handkerchiefs, the road a country track and the sheep like animals from a children's crib. I was not large . . . just a middling man, looking through glass into a Lilliputian landscape, set by some shopkeeper for the summer trade. I did not feel superior . . . only separate, different, faintly resentful, like a child who could not fly out the window with Peter Pan."

Margaret Millar in *Taste of Fears*[7] describes the protagonist, now a patient in a psychiatric hospital, conversing with a police inspector. "She looked into his eyes and quite suddenly he began to recede, to get smaller and smaller until he was no bigger than a doll. She remembered this happening to her as a child, when she was looking at something she especially loved or feared. The experience had always filled her with terror . . . Sands [the policeman]. Ugly little old doll. How wonderfully he was made. Almost human, the way he moved." The conversation continues. Then, "He came back, lifesize."

In *Looking for Mr. Goodbar*,[8] Judith Rossner describes her heroine having sexual intercourse. "Since she didn't respond he got under the quilt and again wrapped himself around her . . . she wanted him to stay there forever, never to move or talk to her or make her look at him. Nor was there any way she could reconcile this desire with the way she felt *now*, actually, except that somehow it got pushed into her mind. Not even her mind. Her *eyes*. She was *seeing* the way she'd felt before while all she was feeling now was the picture of having him hold her. She considered opening her eyes so the *image* of how she'd felt would be replaced by the room's solid objects, but then it didn't seem worth it because the image wasn't even painful any more. She was looking at it through the wrong end of a telescope and it was very far away." (The italicized words are those of the novelist.)

Episodes of psychogenic micropsia experienced by fictional characters are interesting and intriguing as supplements to clinical accounts of the phenomenon. Mention of these fictional descriptions in this report may serve to alert readers further to the occurrences of psychogenic micropsia and to encourage additional investigations by physicians to psychodynamics in patients with micropsia. In addition, micropsia is a reminder of Gulliver among the Lilliputians, enchantingly depicted in the classic work by Jonathan Swift published in 1726.[9]

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Identifying the child with short stature

TO THE EDITOR: The recent article in the *Journal* by Oberfield and Levine (1986; 86:15–21) concerning the child with short stature was a welcomed update, especially regarding growth hormone-related aspects of short stature. The authors properly recommended reference data for attained stature provided by the National Center for

Health Statistics (NCHS) to aid in identifying children with short stature. Nevertheless, the Tanner parent-specific method[1] recommended by the authors for adjusting stature of children for parental stature is inappropriate for American children. This method is based on growth charts for British children, who are systematically shorter than their sex and age counterparts in the United States. Moreover, the population value for midparent stature (average of two parental statures) used by Tanner is considerably shorter than that observed in the United States. Consequently, systematic biases occur when the Tanner parent-specific method is used for evaluating American children.[2]

A parent-specific method that is appropriate for evaluating American children has been developed[2] and recently has been revised for clinical use.[3] These parent-specific adjustment procedures were designed specifically to be used with the NCHS growth charts, and midparental statures were standardized to reflect national levels. Reference tables provide adjustment factors (in centimeters) to be added to or subtracted from the child's measured length (from birth to 3 years) or statures (from 3 to 18 years), according to categories of midparent statures and the age and sex of the child.

Oberfield and Levine suggest using fixed incremental growth rates within age ranges for determining poor or abnormal growth (eg, less than 4.5 cm/yr from 4 years to puberty). More precise evaluation of the relative growth velocity may be provided by using percentile growth increment charts appropriate for American children.[4,5] For example, it is clear that the third percentile of stature velocity is not constant from 4 years of age until puberty. Also, incremental or velocity growth charts allow evaluation of the serial pattern of growth as well as the rate of growth per se at an age.

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In reply. We appreciate the comments by Dr Himes regarding our article. Dr Himes' parent-specific method for correction of children's heights, which has recently been revised for clinical use, allows for correction for parental heights of a child's length or stature from birth to 18 years of age.[1] In this regard, this method allows for the evaluation of a greater age range than is possible with the Tanner parent-specific method. Although the mid-parent height of the British population may be slightly shorter than the American mid-parent height, for practical clinical needs the Tanner charts are useful in determining if a child's height is appropriate for the genetic background.

We have used both Dr Tanner's and Dr Himes' grids to calculate the corrected height percentiles for hypothetical cases and the results for both methods are very similar. Therefore, the reported difference of the mid-parental height in Great Britain versus the United States does not appear to be of clinical significance.

We agree that the recently published Tanner growth curves for American children that reflect average, delayed, or advanced rates of pubertal maturation allow for a "precise evaluation of the relative growth velocity."[2] Furthermore, use of the grids demonstrates that a growth rate of less then 4 cm per year may be a normal growth velocity for a child with delayed pubertal maturation.

We wish to underscore, however, that although such a growth velocity may be normal, pediatricians must carefully follow children with such low growth velocities to determine prospectively if an abnormality in growth exists.

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The Health of the Developing World

By Colin Fraser Brockington, 253 pp. Lewes, Sussex, England, The Book Guild, 1985. (hardcover)

It is now eight years since the World Health Organization and UNICEF sponsored a primary health care conference in the Soviet city of Alma-Ata that marked the beginning of a new approach to health in the developing world.

The reasons why a new approach was needed were clear—medicine was largely by-passing the vast majority of Third World people; the well-appointed hospitals had been built in the capital cities where they served few of the people; and physicians were in short supply. However, there was a paradox in the problems. By the late 1970s, the world had both sufficient medical knowledge and resources to substantially improve the health of all people, not just a few.

Provided that the knowledge and resources are married with organization and used in the right manner, then "health for all" is not just a slogan but a real possibility. At Alma-Ata it was recognized that primary health care has a central part to play in achieving that healthy global society.

The author of this book, Professor Brockington, is Professor Emeritus of Social and Preventive Medicine at the University of Manchester. He describes himself in this book as a firm believer in primary health care, which he considers "the life blood of health in the developing world." Professor Brockington developed the University of Manchester's Department of Social and Preventive Medicine, and has studied social conditions in some 75 countries.

This book builds up the case for the primary health care approach. The author begins by discussing the history of health care, going back to several centuries BC. "The physician was a feature of all early civilizations," he points out, and in some areas the medicine practiced was of a remarkably high standard.

In the book Professor Brockington looks at the rise of health care in Europe and North America over the last 500 years and at the way national systems have developed. He goes on to consider the concept of health and the effect of population growth and migration, geography, climate, and the environment. The middle section of the book deals with development, disease, and demography in the developing countries. The author then turns to the creation of health services in those countries—at organization and planning, staff, hygiene, mass campaigns, epidemic intelligence, and, above all, primary health care.

The author uses the WHO/UNICEF definition of primary health care, describing it as "essential health care made universally accessible to all individuals in the community through full participation of its members by means acceptable to them and at a cost the community and the country can afford."

Prior to 1978, primary health care was slow to take hold in the developing world. However, since the Alma-Ata conference most developing countries have embraced the concept. Although progress has been made, the "life blood" is nonetheless flowing far too slowly for millions of people. Still too many people are not covered by primary health care services. What holds back this bold, life-giving approach?

Organization is undoubtedly a problem in many countries. In order to organize health care among widely scattered communities that are often served by poor communications and perhaps almost cut off from the outside world, the highest of organizational skills are required. Primary health care is not, of course, just about medicine; it is about water and ditches, sanitation and latrines, food and nutrition, hygiene and environmental science, education, contraceptives, and even about the transportation and roads, so that people may have access to facilities. It is about the involvement of local people and the training of some of them to become primary health care workers, and about health experts at the center "letting go" and being willing to delegate to people in the field. It is about people in local communities being seized with a vision of what *might* be, so that they may work to see the dream translated into reality.

Primary health care is "part of a dynamic development process," as stated by the WHO. But to organize the mixed and varied bag of components that help to make a successful system of care was never going to be easy. Not only the Ministry of Health but many other government departments are involved. Coordination is therefore a further essential ingredient. If primary health care has progressed slowly in the past seven years, it is often because it was occasionally assumed that the organizational side was going to be easier than it actually turned out. At least some of the problems are now better known, with the knowledge that what has gone wrong in the past may well be of benefit today.

One problem pinpointed by Professor Brockington is over-centralization and lack of delegation that occurs, he believes, "at all levels." Delegation of sufficient powers from the center to the periphery is "one of the most ne-

glected aspects of a successful infrastructure of health." In many countries, local heads with the necessary technical training, at regional, district, and group levels, have no effective control over the programs in their areas. People in senior positions tend to become absorbed in relatively unimportant detail, for which people at regional, district, or local levels should be responsible. "Centralized power is highly resistant to change," the author correctly points out. It is vital, therefore, to define what functions need to be performed at the center and what should be done at the other levels.

The training of physicians, perhaps at a hospital in the capital city, is again not all it might be. "In hospital," says Professor Brockington, "the student gains little insight into disease as a community problem or into the circumstances that give rise to it." Time must be made for physicians to study people in their environments.

Again, not all persons of the Third World are interested in primary health care ideas. Some Third World communities, for example, put clean water low on their list of priorities. Western medical experts insist that 80% of disease is linked to water, and that the provision of clean water could do more than anything else to revolutionize health maintenance. But the people of a Third World village may simply not recognize unclean water as a problem. In some areas of developing countries where a pump has been provided to bring clean water to the surface, it has been virtually ignored because the "clean water" did not taste as good at the usual supply. In order of priority, Professor Brockington believes that sanitation must be placed first. In Third World villages, however, this rarely appears to happen; even aid agencies like the WHO and UNICEF devote it few resources. People will not be persuaded to maintain sanitary habits unless they first understand the reasoning for such a change and also unless their customs are respected.

The success of any primary health care operation depends on taking the customs of a group of people into consideration. The author sees "the grafting on of new ideas to old beliefs" as the way to make progress. Unless old beliefs are taken seriously, new ideas are unlikely to be accepted; primary health care can only be truly effective if people support it.

Primary health care systems today have a shadow over them that will not be easy to shift—the shadow of foreign debt and a general lack of money. Higher world interest rates have become inextricably bound up with meeting the needs of people. One cause of the foreign debt problems affecting most developing countries is that those countries took out loans expecting to pay a certain rate of interest. Through factors outside of their control, world interest rates soared and higher interest payments had to be made. Many countries have reluctantly raised the money for debt repayments by cutting essential services, such as health care and agricultural support. The human suffering caused by the "Third World debt" has been considerable, especially in the famine hit countries of Africa.

Professor Brockington's book was published during a year when Africa had been hit by the worst famine it had ever experienced. Drought is often said to have caused the famine. This is, however, not the case. Drought in Africa has *triggered* the famine; the *causes* lie deeper. They include the fact that millions of Africans live at the margin of existence; their diet is poor, and they still do not have access to an adequate health service. Disasters may be avoided if primary health care services and the necessary infrastructures are built up; drought does not have to lead to famine. The challenge facing African governments and people, together with sympathetic western country specialists and aid agencies, is to develop primary health care systems so that when the next drought hits Africa—and they tend to come in roughly ten-year cycles—people will survive.

Beyond this interesting book there is need now for a thorough country-by-country review of the results of primary health care. Still not enough is known about the countries that are doing well and about exactly why they are doing well. The cause of primary health care would also be helped if the failures were addressed. Enough progress has been made on the road from the Alma-Ata conference to know that primary health care is the approach that can best make the life blood flow.

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FROM THE LIBRARY

An enemy lurks beneath our feet; his very breath is full of poison; he sends no herald of his coming; he pollutes the water we drink and the air we breathe; he enters our chambers and while we sleep saps the very foundation of our lives; he is ever ready to escape from his prison home, to kill and destroy. His annual victims in this fair city are only numbered by the days of the year. His name is Sewerage. This is not a fancy sketch, but stern, sober truth; and yet, because the victim is killed so quietly and noiselessly in his own house and his pallid features bear no impress of the violent hand laid upon him, the community look on with no sense of horror at the great and unnecessary destruction of human life that is going on.

REPORT OF THE COMMITTEE ON HYGIENE
(*Trans Med Soc State NY* 1875; 402–403)

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In the September 1985 issue the *Journal* began publishing the list of physicians who have generously contributed to the campaign to inform the public about the crisis in medical liability litigation. The names of additional contributors are listed below.

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Sigmund Schutz, MD
Albert M. Schwartz, MD
Jules Leonard Schwartz, MD
William Schwartz, MD
Samuel P. Schwartzfarb, MD
Joseph Schwartzman, MD
George Schwarz, MD
Richard Schwimmer, MD
Bruce Robert Sckolnick, MD
William Doughty Scott, MD
David Jos. Scuccimarra, MD
Thomas Peter Sculco, MD
Robert Stephen Seibt, MD
Reza Seirafi, MD
Henry M. Selby, MD
Kenneth Edwin Seslowe, MD
Shi-Shen Sha, MD
Edward Shaen, MD
Bruce Berner Shafiroff, MD
Niranjan J. Shah, MD
Vasant G. Shah, MD
Jeffrey L. Shakin, MD
Alan Remi Shalita, MD
Sayed Haider H. Shamsi, MD
Benjamin Shankman, MD
William J. Shannon, MD
Stephen Daniel Shappell, MD
Suresh Kumar Sharma, MD
Rameshchandra H. Shastri, MD
K. Joseph Sheedy, MD
Francis Richard Sheehan, MD
Simra Ezra Shein, MD
Michael Carl Shende, MD
Robert A. Sher, MD
Michael J. Shereff, MD
Orrin Howard Sherman, MD
Raymond L. Sherman, MD
Spencer Erwin Sherman, MD
Murray Sherwin, MD
Steven R. Sherwin, MD
Paul W. Shineman, MD
Arthur George Ship, MD
Charles W. Shlimbaum, MD
Joel M. A. Shugar, MD
Oscar J. Siberio, MD
David Sibulkin, MD
Mohammed Y. A. Siddiqui, MD
George Lewis Siegel, MD
Louis Siegel, MD
Mark Ira Siegel, MD
Mark R. Siegelheim, MD
Shepard Silberstein, MD
Scott L. Silver, MD
J. William Silverberg, MD
Richard S. Silverman, MD
Russell Silverman, MD
Henry G. Simmons, MD
Robert Martin Simon, MD
Frank Anthony Simone, MD
Adolf Singer, MD
Jitendra Singh Sisodia, MD
Ellis Norton Sisskind, MD
William Paul Slimbaugh, MD
Albert Benj. Smith, MD
Charles J. Smith, MD
Roy Taylor Smith, MD
Theodore Norman Smith, MD
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Charles W. Socarides, MD
Abram Sohmer, MD
Irving Solomon, MD
Samuel Solomon, MD
Beatrice E. Scott Sommer, MD
Moses Sommer, MD
Anant B. Soni, MD
Toomas Mihkel Sorra, MD
Joseph Sorrentino, MD
George Adam Soufleris, MD
David Dean Speck, MD
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Charles F. Stamm, MD
Sherry F. Stanton, MD
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Richard Boies Stark, MD
John Irwin Starr, MD
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Kenneth Taylor Steadman, MD
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Constantine Stefanides, MD
Martin H. Stein, MD
Paul Stein, MD
Sanford Wilbert Stein, MD
Morris Steiner, MD
Mallory Stephens, MD
Kaethe D. Stern, MD
Mark J. Stern, MD
Marshall Lee Stevenson, MD
Donald H. Stewart, Jr, MD
Jeffrey Stephan Stier, MD
Gerald Stinziano, MD
Gerald Eisner Stone, MD
Peter Wm. Stone, MD
Fred Charles Storm, MD
David George Storrs, MD
Elton Strauss, MD
Robert Lane Strauss, MD
Roger D. Strauss, MD
Ivan Karoly Strausz, MD
Selig Strax, MD
Saleela Suresh, MD
Fouad Surur, MD
Harry Sussman, MD
John David Sussman, MD
Walter Sussman, MD
Pragna B. Sutaria, MD
Joseph David Sutton, MD
John V. Swierat, MD
Carl Richard Szot, MD
Nicolas Tabbal, MD
Joseph R. Takats, DO
Sheila S. Tanenbaum, MD
Gloria K. Tang, MD
Alfred Tanz, MD
James Ziegler Taylor, MD
Richard Rollin Temple, MD
Joseph Tenenbaum, MD
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Jason A. Tepper, MD
Byron Harvey Terk, MD
Richard Newman Terry, MD
Terry Anthony Terzakis, MD
William Edmund Tesauro, MD
Anthony J. Tesoriero, MD
Joseph Salvatore Testa, MD
Jirayr Tezel, MD
Seth Ulric Thaler, MD
Shirish K. Thanawala, MD
Frank Deaver Thomas, MD
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Angeles S. Tiangco, MD
Mitchel Title, MD
Rollin Vital Titus, MD
Victor J. Tofany, MD
Tamer Toklucu, MD
Victoria Toma, MD
Frank Anthony Tomao, MD
Carlos Torres, MD
Miklos Toth, MD
Harold M. M. Tovell, MD
Alexander Traykovski, MD
Byron Morton Treitler, MD
Ajitkumar T. Trivikram, MD
Yu-Hsi Tsai, MD
Chang-Chyi Tseng, MD
Pavritta Man Tuladhar, MD
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Daniel Stanley Turner, MD
Nathan Turner, MD
Arnold Irvin Turtz, MD
Lawrence Henry Tydings, MD
Rusi Ardeshir Udwadia, MD
Jack Lawrence Underwood, MD
Morris Unher, MD
William R. Updegraff, MD
Jerome A. Urban, MD
Hernan A. Urbano, MD
Martin Chas. Ushkow, MD
Frank P. Vaccarino, MD
Courtland Van Deusen III, MD
Ronald L. Van Heertum, MD
Fred Charles Van Natta, MD
Ian Gerald L. Van Praagh, MD
John J. Vasile, MD
James Edward Vaughan, MD
Gary Edwin Veith, MD
Konstantin P. Velis, MD
Stanley M. Vickers, MD
John O. Vieta, MD
Bernardo Ramos Villajuan, MD
Joseph Viola, MD
Herbert Paul Vogel, MD
Howard H. Volan, MD
Harry Gordon Wadsworth, MD
Sasha Wainstein, MD
Kevin M. Walsh, MD
Livia Shang-Yu Wan, MD
Jin-Wen Wang, MD

Irwin Weisbuch, MD
Franklin Stewart Ward, MD
Joseph Noel Ward, MD
John Roger D. Warner, MD
Sheldon R. Watsky, MD
Hyla S. Watters, MD
Lloyd Alfred Watts, MD
Peter Wedeen, MD
Manfred Weichsel, MD
Ruth Helen Weichsel, MD
Donald Weidner, MD
Arthur Wein, MD
Mortimer Weinberg, MD
Andrew Bruce Weinberger, MD
David S. Weinberger, MD
Howard A. Weinberger, MD
Robert S. Weiner, MD
Leonard A. Weingarten, MD
Alan Stephen Weinstein, MD
Clement Weinstein, MD
Gerald Weintraub, MD
Jerome A. Weiss, MD
Jay Michael Weissbrot, MD
Harold Weissman, MD
Sanford G. Weissman, MD
Percyvaldo F. Wendler, MD
Richard Brownson Wenger, MD
Charles A. Werner, MD
Alan Carl Weseley, MD
Coenraad Dirk Westermann, MD
Howard Robert Wexler, MD
Dana M. Wheelock, MD
Philip L. Whitelaw, MD
Wayne Graham Whitmore, MD
Robert E. Wieche, MD
Robert Wielt, MD
Seymour Jerome Wiener, MD
John Burton Wilder, MD
William David Wiley, MD
Roger I. Williams, MD
Donald Alvin Winikoff, MD
Michele L. Winter, MD
Sawarngwong Wirojratana, MD
James Larkin Wise, MD
Max Wolf, MD
Robert Eaton Wolf, MD
Edward A. Wolfson, MD
Claude D. Wolgel, MD
Harvey Wolinsky, MD
Steven Wolinsky, MD
Martin E. Wolpin, MD
Duncan D. Wormer, MD
Ethel Emerson Wortis, MD
Edward J. Wright, Jr, MD
Peter C. Wyer, MD
Saul Yafa, MD
Lawrence A. Yannuzzi, MD
Edward Stanley Yanowitz, MD
Natalie Yarow, MD
Robert P. Yatto, MD
Joel A. Yellin, MD
Woon Bok Rhee Yeon, MD
Sai Hou Ying, MD
V. Prasad Yitta, MD
Stanley S. Yormak, MD
Wilfred Yoslow, MD
Gilbert H. Young, MD
Iven Sheldon Young, MD
Morris Nathan Young, MD
Norman Bernard Yourish, MD
Hsien-Cheng Yu, MD
Ralph Yung, MD
Abraham Yurkofsky, MD
Manuel D. Zane, MD
Bertram E. Zeitel, MD
Peter C. Zervalis, MD
Erwin H. Zimmerman, MD
Joseph George Zimring, MD
Samuel Zinberg, MD
Gary Zisk, DO
Alfred Gerald Ziviello, MD
Nicholas F. Zornek, Jr, MD
Howard D. Zucker, MD
Jerome Zwanger, MD

FINALLY, WE'RE GIVING A KILLER DISEASE SOME OF ITS OWN MEDICINE.

A disease that once put an end to its victims, may soon be put to an end itself.

The disease, carnitine deficiency, destroys the body's ability to produce carnitine, a muscle-fueling substance. Until recently, carnitine deficiency meant certain disability. Often, it meant death.

In the past year, though, carnitine replacement therapy—developed with funding from the Muscular Dystrophy Association—has allowed fully half the patients treated to resume normal lives.

Carnitine replacement therapy is one of the most encouraging developments in MDA's fight against 40 neuromuscular diseases. And for one of those dread diseases, it could be the beginning of the end.

MDA

Muscular Dystrophy Association, Jerry Lewis, National Chairman

NEW PERSPECTIVES IN SCHIZOPHRENIA

Edited by Morton N. Menuck, MD, and Mary V. Seeman, MD. 234 pp, illustrated. New York, Macmillan Publishing Co, 1985. $29.95 (hardcover)

Reading this book was a pleasure. It is well organized and gives concise but rather complete statements on the history of psychiatry's efforts to understand our most baffling psychopathologic syndrome. More than is available in the best textbooks, we are given a series of authoritative statements, and accompanying bibliography, on biologic factors, clinical considerations, and current treatment modalities for schizophrenia. Most of the contributing experts are from Canadian university teaching centers, but American contributors like Cancro, Andreasen, and Hoffman also participated in this symposium that was held at the Clarke Institute of Psychiatry at the University of Toronto in the fall of 1983. Although the nosology is still subject to alternative descriptions, it seems increasingly clear that schizophrenia exists in several forms, that biological determinants are of central importance, that these disorders exist in all sociocultural groups, and that research activity is still needed before we can establish reliable biochemical and psychosocial markers or risk factors.

New biological perspectives create the greatest current excitement since computed tomographic brain scans demonstrated that at least one subgroup of schizophrenic patients have enlarged ventricles and other indications of cortical atrophy and that neuropathologic studies also demonstrate gliosis and neuronal loss in the basal forebrain limbic system and basal ganglia. Moreover, regional cerebral blood flow (RCBF) and positron emission tomography (PET) show that when schizophrenic patients perform intellectual tasks there is a decrease rather than the normal increase in frontal cortex metabolic processes. Other findings suggest that these biologic impairments are more often associated with type II, or poor prognosis, schizophrenia although some clinical studies fail to demonstrate that poor prognosis schizophrenia exists. Long-term studies show that perhaps only as few as 15% of schizophrenics eventually progress to a socially deteriorated course, and that many patients recover to varying degrees after their first five years of illness experience. Even though neuroleptic medication has made a major contribution to the management of acute stages of the illness, it appears that all of our treatment efforts work best with those patients who have a better prognosis from the start, and that it is not possible to identify these good prognosis cases at this time.

A number of interesting facts, or almost established facts emerge, such as the possibility that good prognosis is associated with being female and being left-handed. Another interesting fact stressed by Andreasen is that formal thought disorder does not reliably differentiate schizophrenic from manic patients. Less well known is the finding that, as Andreasen and her colleagues define, formal thought disorders may be found in approximately 15% of persons suffering from major depressive disorders and even among approximately 6% of normals. These are samples of the many thought-provoking ideas the reader can expect to encounter in this excellent book.

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SOCIAL ORGANIZATION OF MEDICAL WORK

By Anselm Strauss, Shizuko Fagerhaugh, Barbara Suczek, and Carolyn Wiener. 310 pp. Chicago, University of Chicago Press, 1985. $25.00 (hardcover)

While physicians may have some discomfort with the use of sociological jargon, Strauss and his colleagues have engaged in a microscopic dissection of the bits and pieces of medical care. Using participant observation techniques, these researchers delineate the art and science of rendering care in minute detail. This text is amply illustrated with case studies, including a particularly well-documented experience of a physician's wife that covered 112 days of hospitalization. What is important here is the fact that this type of study lends weight to the proposition that "caring" may be taught because the specific elements of the work of the providers and the patients are identified. That specificity may then be integrated into the curriculum and taught to both health care providers and to patients.

The investigators state that the shift to the care of people with chronic illness along with the attendant surge in new technology has changed the tasks of medical care teams. Work activities have become more complex and intertwined without the easy solution of a quick injection to resolve the problem. However, hospital staff members still tend to think of themselves as caring for people with acute illnesses. In actuality, the authors believe that their work involves caring for an acute phase of an individual's chronic illness.

Several aspects of the medical care work situation are stressed in this study with emphasis on the following: collective or organized work done within organizational settings; work done along a time line with consequences for workers that in turn affect the line of work (this is labelled a trajectory); changing contingencies that alter the trajectory and its implicated work; problematic trajectories and trajectory phases as well as routine, expectable trajectories and phases; types of work entailed in doing the trajectory work, their relationships, conditions, and consequences; work done on reacting objects (clients); work done on persons who may do some of the trajectory work themselves rather than merely responding to others' work; and work affected by arena disputes and by the ideological positions of the workers themselves.

It should be kept in mind that a diagnosis marks the beginning of a trajectory; the treatment regimen is the trajectory scheme; trajectory managers could be physicians, nurses, or patients; there may be a trajectory for each condition; and there may also be multiple trajectories for individual patients. This trajectory concept covers complete physiological aspects and creates a total plan with all of the impact of each trajectory considered. So much for the translation of medical argot into sociological jargon with the additional overlay of considerations of macroscopic to microscopic impacts and vice versa.

Types of work are identified as machine production, machine tending, and medical production; clinical and envi-

ronmental safety work; sentimental work involving moral rules, building trust, establishing composure, creating awareness, identity, and rectifying insults; and articulation work that is mainly concerned with coordination in getting the job done. Additional consideration is given to error work, body work, information work, and negotiative work. Furthermore, all of these types of work may be engaged in by the providers as well as the patients.

At times, the style of writing may be difficult to follow unless the reader remembers the basic trajectory concepts. This is not necessarily hard to do if one concentrates on the work of medical care. Nevertheless, the style becomes secondary as the vivid narratives of actual case studies are used to demonstrate the issues. Even though the underlying premises have been stated on numerous occasions, this book is still worth reading. These researchers spent four years gathering data from a variety of medical care work sites; medical care workers will readily recognize themselves in these vignettes. It should be obvious that this book may be added to the body of literature used for adjusting medical care trajectories to the changes in the nature of the ailments being worked on by medical care providers. Critics may note that the work details are commonplace and automatic for experienced providers. Despite that, this book is worth reading because these experienced investigators have identified the particular tasks and specified the nature of the recommended changes in the health care delivery system.

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CARDIOLOGY 1985

Edited by William C. Roberts, MD. 500 pp, illustrated. New York, Yorke Medical Books, 1985. $55.00 (hardcover)

This book represents the fifth in an annual series of reviews of the current cardiac literature. It reviews most of the pertinent articles published in the major medical journals in 1984. In essence, it is similar to a journal club review, since each of the seven authors have been assigned specific journals rather than specific subjects to review.

The nine chapters are categorized by etiological subjects, except for the third chapter on arrhythmias, conduction disturbances, and cardiac arrest, and the last two chapters that relate to congestive heart failure and miscellaneous topics—exercising and exercisers, obesity, cardiac or pulmonary transplantation, and the mechanical heart.

The chapters having major etiological designations include those on coronary artery disease, acute myocardial infarction and its consequences, systemic hypertension, valvular heart disease, myocardial heart disease, and congenital heart disease.

The distinguished editorial board is headed by the editor in chief of the *American Journal of Cardiology*, William C. Roberts, MD, and the editor in chief of the *American Heart Journal*, Dean T. Mason, MD, and includes two other adult cardiologists, a pediatric cardiologist, and two cardiac surgeons. In addition, each in his own right has contributed significantly to the cardiac literature.

The journals chosen for review include all of the major American cardiac journals, the *British Heart Journal*, and several thoracic surgical journals as well. The papers reviewed are summarized in detail to demonstrate the significance of the information and its comparability to other papers on the same subjects, and yet give only pertinent data to the reader. The references are clearly identified and appear at the end of each chapter. Altogether, summaries of 761 papers have been included in this book.

In the section on arrhythmias, many of the newer drugs used for control of both supraventricular and ventricular arrhythmias are discussed. In addition to cardiac arrest, reviews of such subjects as sudden infant death syndrome, syncope, sleep apnea syndrome, bundle branch block, pacemakers, and cardioverters are included. Under the title of "Congestive Heart Failure," newer drugs used to reduce pre-load and afterload are discussed and compared.

This book serves as a ready reference to update oneself quickly about current thinking in the various fields of cardiac disease. It is useful as a base on which to peruse the literature on a given cardiac subject. Therefore, it would be particularly useful for students of cardiology, internists, and family physicians who deal with cardiac problems but do not have the time required to follow the current journal literature.

Quite coincidentally, the present reviewer has found each of the previous four year books uniformly informative and would recommend them all as useful references.

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THE ASTHMA HANDBOOK. A COMPLETE GUIDE FOR PATIENTS AND THEIR FAMILIES

By Stuart H. Young, MD, Susan A. Shulman, and Martin D. Shulman, PhD. 272 pp, illustrated. New York, Bantam Books, 1985. $3.95 (paperback)

The authors set out to write a book for the layman that would encompass the topic of allergies and asthma in children and adults. They obviously wanted to avoid convoluted medical terms and physiologic descriptions. Their purpose was to answer the many questions that are asked of physicians by young patients and their parents. At the outset, the authors are identified as a physician who specializes in allergic medicine (Young) and two professional writers (Shulman and Shulman). Dr Young's first-hand input makes the book easily readable. Its anecdotal quality, based on his years of clinical experience, allows the reader to "be in the doctor's office" hearing him tell his patients what they need to know about the subject.

The authors are up-to-date with regard to the various new modes of pharmacologic therapy that have recently become available. The topics of asthma and allergic rhinitis are dealt with in simple terms. Yet for the professional, there is a great deal that may be learned from these discussions. The confusing problem of urticaria is presented in a very straight-forward manner. I have already used this section to assist me in my own practice.

After the introduction—that outlines the composition of the book—the authors then discuss various aspects of atopy and punctuate the topics of asthma, allergic rhinitis, food allergies, and urticaria with case histories. When diet is the issue, as it is with food allergies, methods of dealing with the offending foods are offered. One wishes that the authors would have provided dietary menus because patients so often ask about what they may eat rather than just about what they cannot eat.

I especially appreciated their chapter entitled "Asthma at Special Times" and its superb discussion of the disease during pregnancy. The discussion of hypnosis and asthma (a field in which Dr Young has considerable expertise) is part of a whole chapter devoted to stress management and the disease. The presentation is a thoughtful one from which a patient may glean much practical information.

It is not the accuracy of this book that is its major strength. What sets it apart from others that have dealt with the topic is the inclusion of the allergists' remarks to patients. Dr Young's capacity to personalize his comments allows the reader to absorb a great deal of information. I have heard many parents tell me that they literally could not put this book down.

In short, while one might say that this book is not a scientific endeavor, it is nevertheless essential to the person with allergies or asthma, or to the parents of children with allergies or asthma. But it could be said that there are physicians who "don't believe in allergies," and for these individuals this book might well be an eye opener.

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RENAL PATHOPHYSIOLOGY

Third Edition. By Alexander Leaf, MD, and Ramzi S. Cotran, MD. 418 pp, illustrated. New York, Oxford University Press, 1985. $18.95 (softcover)

Once maintenance dialysis and kidney transplantation were shown to extend life and effect rehabilitation in irreversible renal failure, a rationale for why kidneys fail assumed great importance. Uremia may be acute or chronic. It may occur as a component of systemic disease such as diabetes mellitus, or as an isolated kidney disorder as in allergic interstitial nephritis.

Leaf and Cotran have logically organized and succinctly presented an initial approach to how the kidney works in health and what happens when diseases of the kidney alter body composition. Originally prepared as an outline for Harvard medical students, this 418 page paperbound book is divided into 14 chapters beginning with renal circulation and renal physiology and ending with vascular diseases of the kidney, renal hypertension, pyelonephritis, and other tubulointerstitial diseases. Having grasped the contents of renal pathophysiology, a student or practitioner is well prepared to assess the meaning of abnormal screening tests for renal function and acid-base balance. The value of teaming a pathologist (Cotran) with a physiologist (Leaf) becomes evident in their superb exposition on renal artery stenosis, necrotizing vasculitis, and malignant nephrosclerosis, which would stand alone as a fine monograph.

It would have been helpful to expand what is a too brief discussion of the role of glomerular hyperfiltration as a cause of progressive renal injury as well as the possible contribution to renal damage resulting from a high protein diet usual to American hamburger addicts. I enjoyed this book and was happy to give my copy with a positive endorsement to my daughter who is now in the midst of a second-year course in pathophysiology.

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THE COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS COMPLETE HOME MEDICAL GUIDE

Edited by Donald F. Trapley, MD, Robert J. Weiss, MD, Thomas Q. Morris, MD, Genell J. Subak-Sharpe, MS, and Diane M. Goetz. 911 pp. New York, Crown Publishers, Inc, 1985. $39.95 (hardcover)

This book is a remarkable compilation that is intended to do more than just advise readers about what to do when they become ill. Its purpose is to inform readers not only about coping until help arrives, but also about preventing illness, maintaining good health, and obtaining the most out of the medical care system. This is a fairly large order but one that is superbly met by five editors and more than sixty individual contributors who are faculty members of Columbia University's College of Physicians and Surgeons. Despite the large number of contributors, there is a cohesive uniformity to the prose, brought about through the efforts of Genell J. Subak-Sharpe, the editorial director who is also a leading medical journalist.

The book is divided into eight sections: The Nature of Health and Medicine; What To Do Until the Doctor Comes; Your Body and How It Works; Maintaining Personal Health; Disease Treatment and Prevention (which is the bulk of the book, covering 406 of the 911 pages); Drugs and Their Use; Directory of Resources; Medical Terms and Their Meanings; four appendices, and an index. In addition, an atlas of major organ systems is provided.

This is not only a comprehensive book but also one that is concise. Line drawings, charts, and graphs emphasize important points. Unlike a number of other home medical guides, this one is written by specialists in various subject areas, which gives it substantial authority.

It is clear that the editors have made efforts to simplify complex technological concepts and issues. And for the most part, they have eminently succeeded at this. However, in some sections, the narrative becomes complex and will require effort for nonmedical readers to follow. Fortunately, these sections are few.

The authors and editors have presented up to date state-of-the-art information on prevention, diagnosis, and treatment of a wide range of disabilities. The have also included information about current theoretical medical concepts and insights into future developments. Complementing this aspect of the book is sound advice about obtaining health resource information and selecting a physician, hospital, and nursing home. Readers are also provided with clear insights into how the health care system works.

This book superbly succeeds where many others have failed because it taps the knowledge of eminent specialists, conveys it in language understandable to laymen, and presents it in an ordered and integrated fashion. Much of the credit for this must go to the editors, and particularly to Genell Subak-Sharpe, the editorial director who oversaw the entire project from its inception.

Comprehensive and authoritative, current and easy to understand, this book is highly recommended for a wide audience of lay readers.

PASCAL JAMES IMPERATO, MD
Editor

FDA Reports proposed priorities for 1988

Improving new drug review and the reporting mechanisms for adverse reactions to drugs or medical devices, and addressing the problem of health fraud were the three activities most often recommended by physicians and other health professionals for increased attention from the Food and Drug Administration (FDA) in 1988.

A total of 155 health professionals, representing medicine, veterinary medicine, pharmacy, dentistry, and other allied health professions participated in the FDA's discussion of priorities for the fiscal year 1988. The information was collected from ballots distributed to health professionals, consumers, state officials, trade associations, small businesses, and FDA policy board alumni. The results do not absolutely determine the agency's priorities, but rather are provided to the commissioner and managers for planning and budgeting use.

The health professionals were in agreement with the other interest groups in selecting new drug review as a high priority; however, most other groups determined health fraud as being of greater importance than did the health professionals and did not include adverse drug/device reporting in their top three priorities. The health professionals did concur with other interest groups in selecting nutrition and internal management as items for suggested de-emphasis.

The participants in the survey were asked to make their judgments on the ten FDA action plan goals: new drug review, medical devices, adverse drug/device reporting, risk assessment, risk management, food safety, nutrition, new technology, health fraud, and internal management.

American College of Physicians limits use of funds for FMGs

The American College of Physicians has determined that public funds should not be used to assist US citizens who attend unaccredited foreign medical schools or to support the postgraduate residency training of graduates from such schools.

"In the past, public funds, such as Medicare, which are usually allocated for patient care services, have been used to support the graduate medical education of both US citizens and foreigners in the nation's hospital-based residency programs," said John R. Ball, MD, JD, associate executive vice president of Health and Public Policy.

Many foreign medical graduates (FMGs) come to the United States for required clinical residency training. However, of the 5,203 US citizen FMGs, only 4% passed the Foreign Medical Graduate Examination in the Medical Sciences in 1985. The test is administered to measure medical knowledge in basic and clinical sciences and clinical skills of applicants to US medical residency programs. Of the approximately 20,200 foreign-born FMGs who were tested in 1985, 18% successfully completed the examination.

"Because of this poor performance record, especially for US citizens who attend foreign medical schools, the current shortage of public funds, and a possible surplus of physicians in the United States, the ACP believes that the public monies, currently used to support graduates of foreign medical schools in US clinical residency programs, should be eliminated," Dr Ball reported.

The ACP encourages support for providing graduate medical education for a limited number of foreign students who enter the country as part of exchange programs. This education should be provided in the way of services needed in the students' native country, and the funding for such education should come from a source other than patient care revenues, according to Dr Ball.

The Dr Michael Kennéy Memorial Lecture

The former director of the Centers for Disease Control, William H. Foege, MD, MPH, was the second annual Dr Michael Kennéy Memorial lecturer at the State University of New York Health Science Center at Brooklyn on April 18, 1986. Dr Foege, who is currently President of the American Public Health Association, spoke on "The Revolution in International Health."

The lecture was established in 1984 through an endowment by Dr Kennéy's widow, author Lona S. Kennéy. It is co-sponsored by the Departments of Preventive Medicine and Community Health and Pathology and the Alumni Association of the College of Medicine. The lecture honors the late Dr Michael Kennéy who died in 1982. A noted pathologist and tropical disease expert, Dr Kennéy served for many years in the Congo (now Zaire) and in British Guiana (now Guyana). In 1948 he became Chief of Microbiology of the Bronx Veterans Administration Hospital and later served as Chief of Clinical Pathology at the New York City Veterans Administration Hospital. In 1968 he became Professor of Pathology at the Downstate Medical Center where he established and directed a new tropical disease and parasitology service and laboratory. His now famous color atlas, *Patho-Parasitology*, was published in 1973.

Physicians receive awards

Two prominent New York physicians were presented awards for outstanding service by the New York Academy of Medicine on April 9.

The Academy Plaque for 1986 was presented to Duncan W. Clark, MD, for outstanding service to both the Academy and the community. Dr Clark's service to the Academy spans 35 years. He served the Academy in many capacities, as a member of the council and as both vice president and president. Dr Bernard J. Pisani, the current president of the Academy and a former president of the Medical Society of the State of New York, presented the plaque to Dr Clark along with Mary Ann Payne, MD, the

Academy's treasurer who also delivered the presentation speech.

Dr Clark, who received his MD degree from the Long Island College of Medicine 50 years ago, distinguished himself as an internist, medical educator, and administrator. He completed his internship at Brooklyn Hospital, his medical residency at Kings County Hospital, and was a fellow in internal medicine at Yale University. After a brief period in private practice, Dr Clark entered full time academic medicine at the Long Island College of Medicine where, at the age of 37, he became the youngest physician ever to serve as dean of a medical school. In 1951 he became professor and chairman of the school's Department of Environmental Medicine and Community Health, a position he held until 1978. A former president of the Association of Teachers of Preventive Medicine, he served as a consultant to the US Public Health Service for 20 years. He is the senior editor of Clark and MacMahon's *Preventive and Community Medicine*, one of the most widely used texts in the field. Dr Clark is currently Professor Emeritus of Preventive Medicine and Community Health at the State University of New York Health Science Center at Brooklyn.

Also honored by the Academy was Irving S. Wright, MD. Dr Pisani presented Dr Wright with the 1986 Medal of the New York Academy of Medicine for his outstanding contributions to science and medicine.

NEWS BRIEFS are compiled and written by Sandra Cirincione.

Dr Wright is distinguished for his work in the fields of vascular disease and thromboembolism. He was one of the pioneers in using anticoagulants to prevent and treat the thromboembolic complications of myocardial infarction, rheumatic heart disease, and selected patients with cerebral vascular disease.

Dr Wright served for 12 years as Founding Chairman and Secretary General of the International Committee on Blood Clotting Factors (later known as the Committee on Haemostasis and Thrombosis.) He developed the Roman numeral system for the identification of basic blood clotting factors that was officially adopted in 1959 and has since been used throughout the world.

Dr Wright is also in the forefront of research on aging. He is the president of the American Federation for Aging Research, a national organization whose objective is to develop support and funding for basic and clinical research in the mechanisms, prevention, and treatment of the aging process and its complicating associated diseases.

Another New York physician who received honors was Eli A. Friedman, MD, professor of medicine and chief of the Renal Diseases Division, State University of New York Health Science Center at Brooklyn. Dr Friedman is the 1986 recipient of the Hoenig Award, a coveted award in the field of kidney disease presented by the National Kidney Foundation of New York and New Jersey. Dr Friedman is a past chairman and current member of the Medical Advisory Board of the National Kidney Foundation of New York and New Jersey.

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Position of the Medicine/Business Coalition of New York on medical liability

The Medicine/Business Coalition of New York State recently issued the following overview concerning medical liability.

The medical liability problem is part of an expanding area of concern with respect to the cost and unavailability of liability insurance. It affects not only hospitals and physicians in the medical area, but also midwives and other providers of medical and custodial care as well. There is similar concern with respect to municipal liability, product liability, and environmental liability.

The broader problem needs to be kept in mind so that the civil justice system—the process for resolving disputes among parties in our society—may be reformed in such a way as to have the greatest possible applicability. However, such a broadening of the problem may not expedite solutions in the medical liability area.

The medical liability tort reform measures introduced or strengthened in New York State in the spring of 1985 are commendable. But in addition, the following changes are needed:

- A cap on pain and suffering awards. Limits on the amounts recoverable for noneconomic losses are supportable since such damages are highly subjective, resulting in widely differing awards in similar circumstances. Limits provide some equity between awards and reduce malpractice premiums. The coalition does not propose limits on economic damages (including the cost of medical and rehabilitation care and lost wages) that may be determined on a reasonably objective basis.
- The elimination of lump sum payments representing the estimate of anticipated future medical costs. This is to be replaced by a managed pooled trust fund with the concept of medical case management in control of the distribution of payments.

The coalition does not support the excess liability coverage provisions passed by the New York State Legislature in 1985. The proposal does not address the underlying problems and, in fact, could be viewed as decreasing physicians' incentives for good risk management and encouraging higher jury awards. The coalition supports the availability of excess liability coverage at the expense of the medical provider.

The coalition also does not support proposals to spread the financial base for funding medical liability costs except to the extent indicated in the proposal concerning anticipated future medical costs. It believes such an approach decreases the incentives for good risk management on the part of the medical community by insulating them from the real costs.

It is essential that standards of medical care be based on quality rather than quantity. The medical profession must be willing to participate with their colleagues in the development of treatment principles that may serve as guidelines for the practicing physician. The choice is to either practice within criteria established by colleagues in clinical practice and academic and research areas, and be in a strong posture with respect to defending liability charges or to follow a more individualized pattern of practice that may be challenged by "expert witnesses" in the courtroom. For example, documentation of the medical risks and benefits of a test or procedure will add substance to its defense, where such information is available.

With sufficient data collection from many sources in the private and public sector, it should be possible for the medical community (physicians and hospitals) to reach a consensus of basic principles on many medical treatments based on successful outcomes rather than personal biases and habits. Physicians should welcome the opportunity to practice their profession, making judgments based on their collective experience, and free from the burden of defensive medicine. Efforts should be made to strengthen and expedite the professional disciplinary system so that health professionals who have been judged to be functionally impaired or incompetent shall be removed from patient care by having their license to practice suspended or rescinded.

Some individuals are advocating that the State take over the medical liability insurance companies (considered bankrupt) and their assets. Insurance with the State entity would be mandatory and the business would be run on a pay-as-you-go (including claims-made) basis. The coalition does not support such an approach that fails to fund for anticipated costs on an acceptable basis.

The coalition supports incentives for data collection and analyses (actuarial studies, practice patterns, utilization, judgments, etc) on a systematic basis. It finds it difficult to believe that after all the years of experience accumulated in the various states, definitive answers are still lacking as to the most effective measures to cope with the problem.

The coalition endorses the idea that the following special considerations be explored more fully: binding arbitration; a no-fault system; experience rating of physicians and hospitals; and adverse outcomes versus negligence.

MEDICAL SOCIETY NEWS is written by Sandra Cirincione.

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Ernest Henry Carhart, MD, Syracuse. Died March 8, 1986; age 61. He was a 1955 graduate of the State University of New York Upstate Medical Center, Syracuse. Dr Carhart was a Diplomate of the American Board of Family Practice and a member of the American Academy of Family Practice, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Abraham A. Clahr, MD, New York. Died March 1986; age 85. Dr Clahr was a 1925 graduate of the University of Maryland School of Medicine, Baltimore. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Gerald Charles Cooney, MD, Syracuse. Died November 19, 1985; age 89. He was a 1920 graduate of the State University of New York Upstate Medical Center, Syracuse. Dr Cooney was a Diplomate of the American Board of Internal Medicine and a member of the Academy of Medicine, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Ruth Foster Crabtree, MD, Newburgh. Died February 15, 1986; age 85. Dr Crabtree was a 1924 graduate of Cornell University Medical College, New York. She was a Fellow of the American College of Anesthesiologists and a member of the American Society of Anesthesiologists, Inc, the Medical Society of the County of Orange, and the Medical Society of the State of New York.

James Gordon Derr, MD, Syracuse. Died December 21, 1985; age 87. Dr Derr was a 1925 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a Diplomate of the American Board of Surgery, and a member of the Academy of Medicine, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Clara Flora D. Diasio, MD, Richmond, Virginia. Died March 23, 1986; age 83. Dr Diasio was a 1929 graduate of the New York Medical College, Flower and Fifth Avenue Hospital. She was a member of the Medical Society of the County of Genesee and the Medical Society of the State of New York.

Israel Gitlitz, MD, Monsey. Died March 17, 1986; age 71. He was a 1942 Licentiate of the Royal College of Physicians of Edinburgh. Dr Gitlitz was a member of the Academy of Medicine, the American Geriatrics Society, the American Public Health Association, the Medical Society of the County of Rockland, and the Medical Society of the State of New York.

Leo Gourvey, MD, St Petersburg, Florida. Died December 18, 1985; age 87. Dr Gourvey was a 1922 graduate of the Kazan Medical Institute, Kazan, USSR. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Francis Hess, MD, Rochester. Died February 7, 1986; age 85. Dr Hess was a 1926 graduate of the Medizinische Fakultät der Universität, Wien. He was a member of the Academy of Medicine, the American Academy of Family Practice, the Medical Society of the County of Monroe, and the Medical Society of the State of New York.

Arthur Howard, MD, Johnstown. Died February 25, 1986; age 72. He was a 1944 graduate of the Chicago Medical School. Dr Howard was a Fellow of the American Academy of Family Practice and a member of the Pan American Medical Association, the American Geriatrics Society, the Medical Society of the County of Fulton, and the Medical Society of the State of New York.

David John Impastato, MD, Pasadena, California. Died February 28, 1986; age 83. He was a 1928 graduate of the George Washington University School of Medicine, Washington. Dr Impastato was a Diplomate of the American Board of Psychiatry and Neurology and a member of the Academy of Medicine, the New York Neurological Society, the American Academy of Neurology, the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

Wladimir Kokorudz, MD, Owego. Died February 27, 1986; age 70. He was a 1943 graduate of the Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin. Dr Kokorudz was a Fellow of the American Academy of Family Practice and a member of the Medical Society of the County of Tioga and the Medical Society of the State of New York.

Carl Otto E. Lindbeck, MD, Jamestown. Died February 23, 1986; age 90. Dr Lindbeck was a 1923 graduate of Rush Medical College, Chicago. He was a member of the Academy of Medicine, the Medical Society of the County of Chautauqua, and the Medical Society of the State of New York.

Thomas Francis Joseph May, MD, Forest Hills. Died March 3, 1986; age 78. He was a 1934 graduate of Georgetown University School of Medicine. Dr May was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, a Diplomate of the American Board of

Obstetrics and Gynecology, and a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Benjamin Miller, MD, East Durham. Died January 26, 1986; age 76. Dr Miller was a 1935 graduate of the University of Edinburgh Faculty of Medicine. He was a member of the American Academy of Family Practice, the Medical Society of the County of Greene, and the Medical Society of the State of New York.

William E. Morris, MD, Amsterdam. Died December 12, 1985; age 67. He was a 1943 graduate of the Albany Medical College of Union University. Dr Morris was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Urology, and a member of the American Urological Association, the Medical Society of the County of Montgomery, and the Medical Society of the State of New York.

Edward E. Powers, Jr, MD, Rome. Died February 25, 1986; age 70. Dr Powers was a 1951 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a member of the Academy of Medicine, the American Academy of Family Practice, the Oneida County Medical Society, and the Medical Society of the State of New York.

Arthur Isaac Rosenthal, MD, Woodmere. Died March 1986; age 83. He was a 1929 graduate of the University of Edinburgh Faculty of Medicine. Dr Rosenthal was a Fellow of the American College of Anesthesiologists and a Diplomate of the American Board of Anesthesiology. His memberships included the Academy of Medicine, the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Simon Smelensky, MD, Brooklyn. Died December 28, 1985; age 81. Dr Smelensky was a 1928 graduate of New York University College of Medicine. He was a Fellow of the American Academy of Family Practice and a member of the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Richard Leo Sullivan, MD, Manlius. Died October 1, 1985; age 71. He was a 1939 graduate of the State University of New York Upstate Medical Center, Syracuse. Dr Sullivan was a Diplomate of the American Board of Otolaryngology and a member of the American Academy of Otolaryngology, the American Laryngological, Rhinological, and Otological Society, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Henry E. Vogel, MD, Buffalo. Died March 7, 1986; age 81. He was a 1931 graduate of the University of Illinois College of Medicine, Chicago. Dr Vogel was a Fellow of the American College of Surgeons and a member of the American Society of Abdominal Surgeons, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Jess T. Wallace, MD, Flushing. Died March 14, 1986; age 88. Dr Wallace was a 1923 graduate of Columbia University College of Physicians and Surgeons, New York. Dr Wallace was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Medical Society of the County of Kings and the Medical Society of the State of New York.

Carl Weiss, MD, Marathon. Died November 1, 1985; age 81. Dr Weiss was a 1929 graduate of the Medizinische Fakultät der Universität, Wien. He was a Fellow of the American College of Chest Physicians and a member of the New York County Medical Society and the Medical Society of the State of New York.

Elias Walrath Young, MD, Goshen. Died February 28, 1986; age 80. Dr Young was a 1933 graduate of Albany Medical College of Union University. He was a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

Guidelines for authors

Originality

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089-1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

Preparation

An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), an abbreviated title of no greater than 40 spaces for use as a running foot, and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

Categories

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

Figures

The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

References

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

References should be indicated in the text by superscript numbers following the name of the author (eg, Smith[2] reported two cases).

The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear on the text. When there are six or fewer authors, all should be listed; where there are seven or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83:925-927.
2. McGuigan JE. Peptic ulcer. In: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD, eds. *Harrison's Principles of Internal Medicine.* New York, McGraw-Hill, 1983, pp 1697-1712.

Review

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

Address correspondence to Pascal James Imperato, MD, Editor, *New York State Journal of Medicine*, P.O. Box 5404, 420 Lakeville Road, Lake Success, NY 11042.

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July 18–20. **American Society for Dermatologic Surgery: Techniques and Current Concepts in Dermabrasion, Chemical Peel and Soft Tissue Augmentation.** 15 Cat 1 Credits. The Copley Plaza. Info: A.S.D.S. Office, 1567 Maple Ave, Evanston, IL 60201. Tel: (312) 869-3954.

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July 10–12. **9th National Conference on Pediatric/Adult Allergy.** 20 Cat 1 Credits. Four Seasons Hotel, Toronto. Info: Rayna Saville, Coordinator, Pediatric Continuing Medical Education, Children's Hospital of Buffalo, 219 Bryant St, Buffalo, NY 14222. Tel: (716) 878-7630.

ENGLAND

July14–18. **The Impact of Technology and Social Change on the Provision of Health Care.** Castle View, Dudley, West Midlands. Info: International Health Care Conference, Adult Registrar, Donaldson Brown Center for Continuing Education, Virginia Polytechnic Institute, Blacksburg, VA 24061. Tel: (703) 552-8322.

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PROFESSIONAL MISCONDUCT DEFENSE; DISCIPLINARY LAW; SCIENCE LAW: Irwin Birnbaum and Paul Giancola, Lawyers, Mony Plaza II, Syracuse, New York 13202, (315) 422-0246 (In New York, (800) 358-8568). Law practice limited to Biotechnology Law, Litigation, and Disciplinary Proceedings. Principals have extensive scientific litigation experience or training, and hold adjunct law college appointments in scientific litigation. Irwin Birnbaum, LLB is a former principal Assistant District Attorney for Onondaga County, with extensive experience in both civil and criminal litigation involving the forensic sciences. Paul J. Giancola, JD is a licensed physical therapist, with extensive civil litigation experience. Partners have lectured at medical schools, engineering colleges, and at numerous seminars and meetings. Irwin Birnbaum is the Chair of the Roscoe Pound Commission on Professional Responsibility. The partners' vitae and bibliographies are available on request. Birnbaum and Giancola, Lawyers. In New York, (800) 358-8568. Outside New York, (315) 422-0246. Mony Plaza II, Syracuse, New York 13202.

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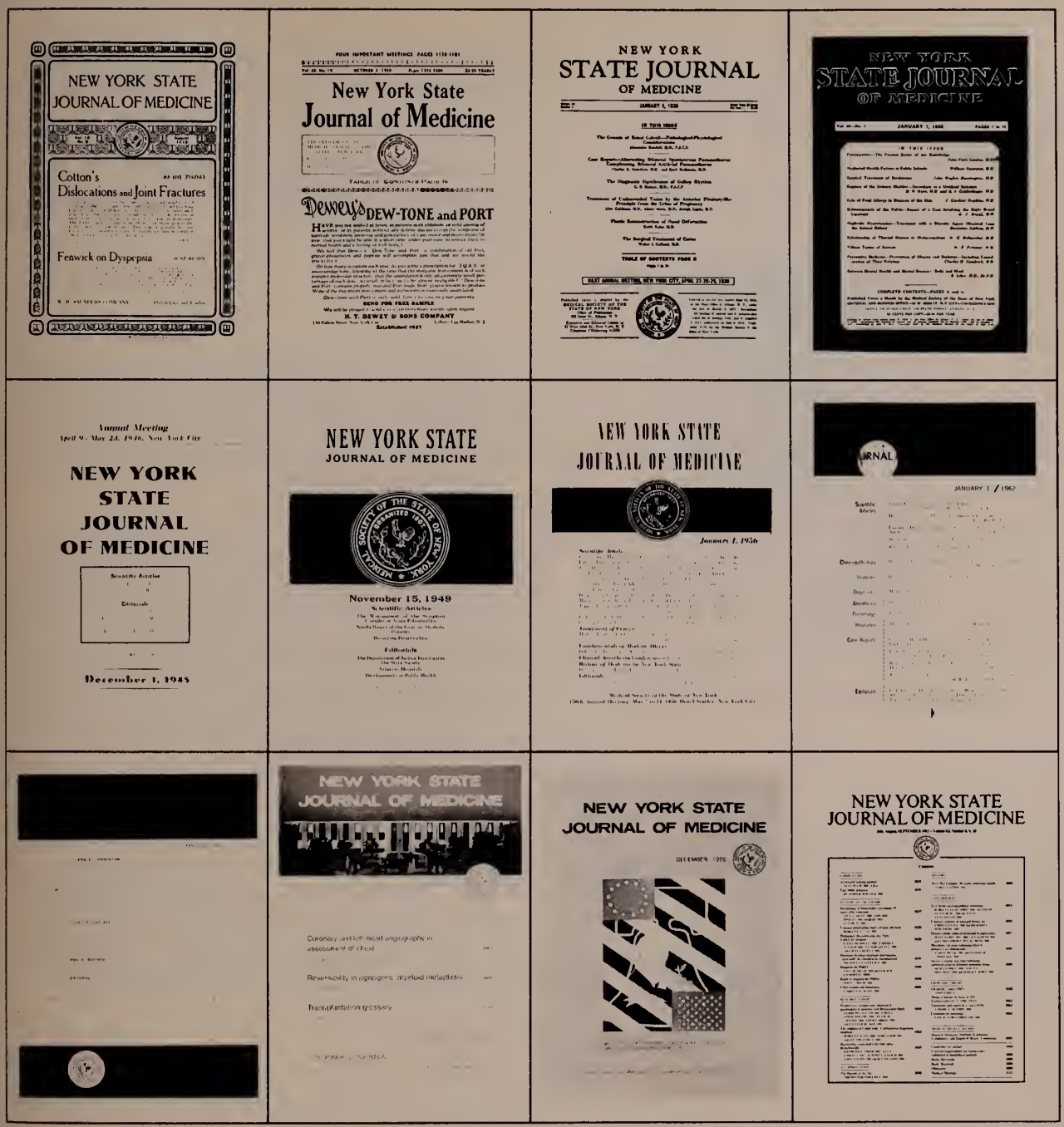

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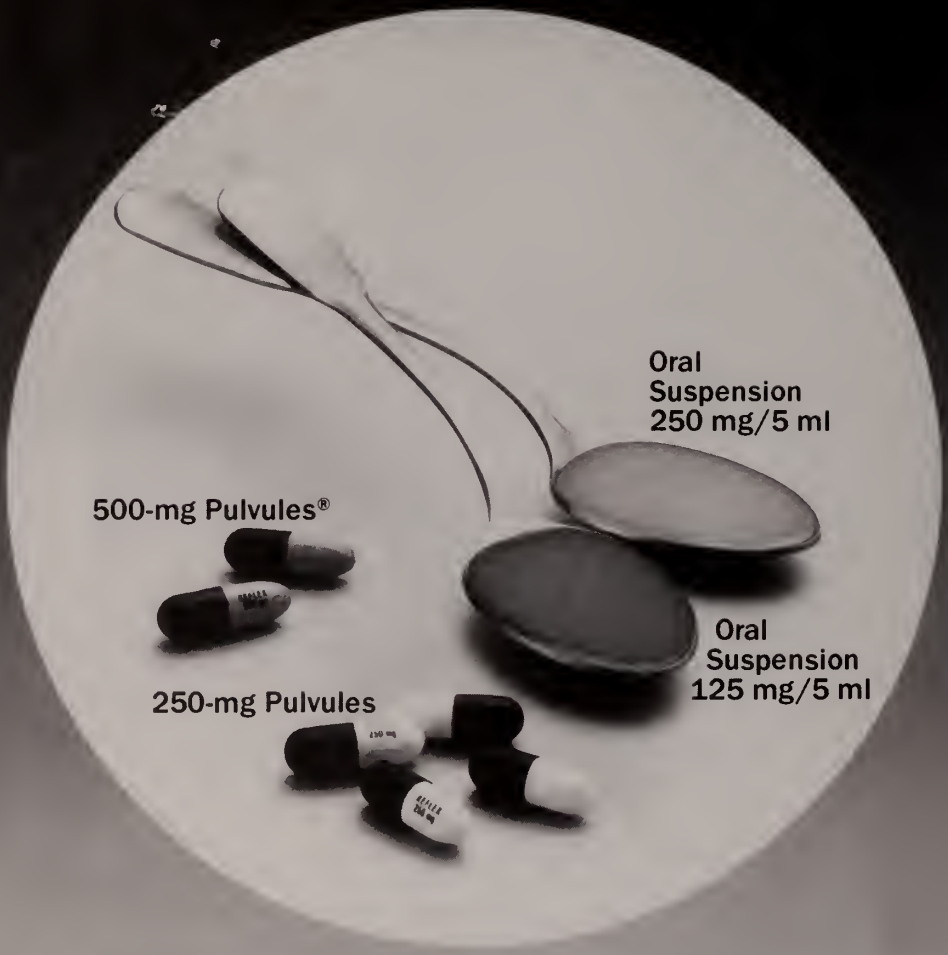

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2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes, however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM (diltiazem hydrochloride) in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope
Nervous System	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia
Gastrointestinal	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH
Dermatologic	Pruritus, petechiae, urticaria, photosensitivity
Other	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme, leukopenia, and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy** — CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

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CARDIZEM 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other. Issued 4/1/84

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(See *Warnings.*) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecomastia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984. 2385

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MEETINGS AND LECTURES

The New York State Journal of Medicine *cannot guarantee publication of meetings and lectures unless the information is submitted at least three months prior to the event.*

AUGUST 1986

AROUND THE STATE

MANHATTAN

Aug 15–17. **A Basic Review of Cardiology.** 15 1/2 Cat 1 Credits. Grand Hyatt Hotel. Info: Tampa Tracings, PO Box 1245, Tarpon Springs, FL 33589. Tel: (813) 937-7370.

Aug 16–19. **Internal Medicine Board Review Course.** Grand Hyatt Hotel. Info: American College of Physicians, PO Box 7777-R-0510, Philadelphia, PA 19175.

SUFFOLK

Aug 2–3. **Current Issues in Mental Health.** 6 Cat 1 Credits. Southampton. Info: Ms Jane Smyth, Administrator, Hampton Summer Institute, 128 East 56th St, Box 430, New York, NY 10022. Tel: (718) 268-4952.

AROUND THE NATION

CALIFORNIA

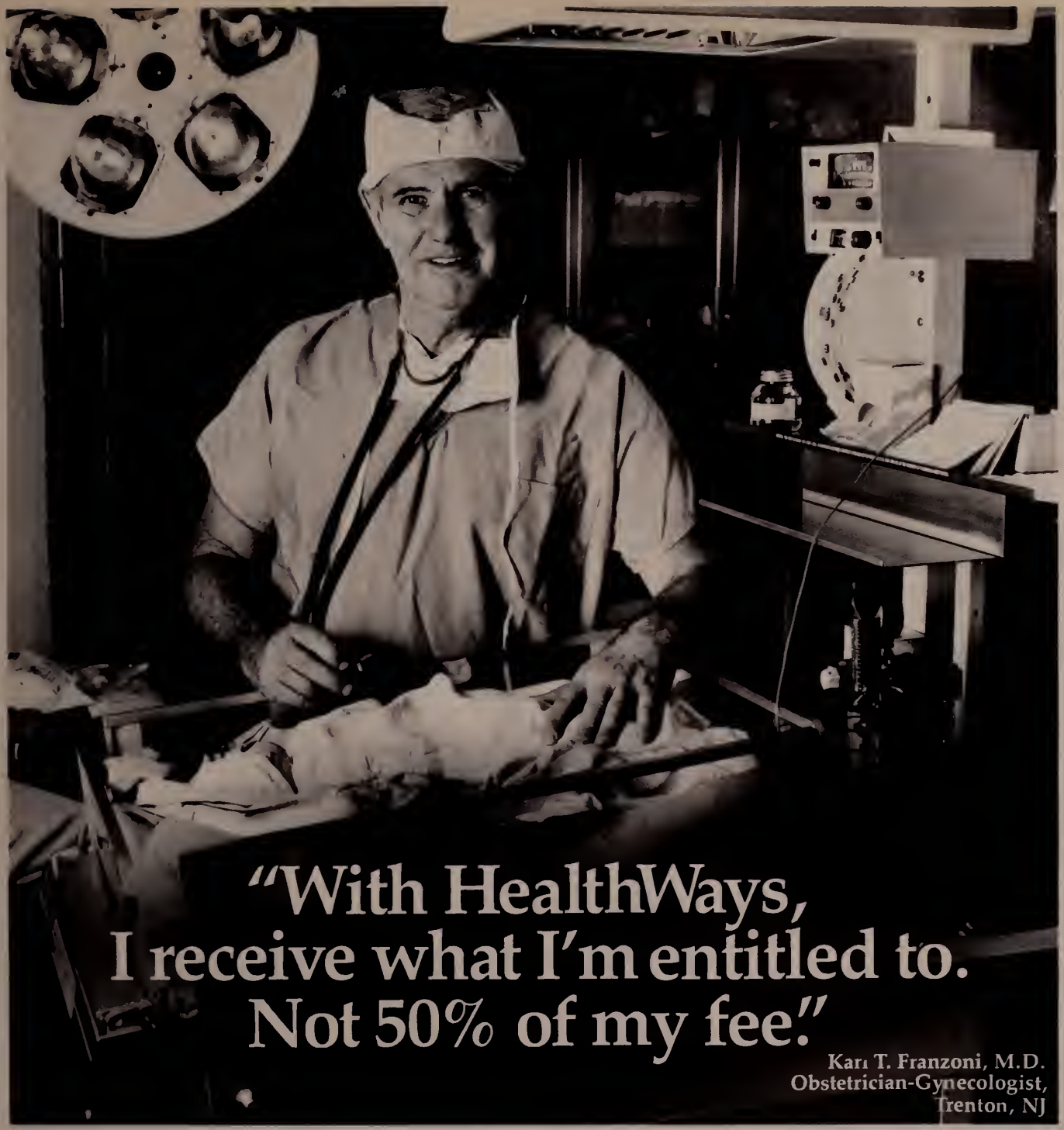
Aug 7–9. **Clinical Management of the Elderly Patient.** 14 Cat 1 Credits. Fairmont Hotel, San Francisco. Info: The Health and Education Council, Inc, 7201 Rossville Blvd, Baltimore, MD 21237. Tel: (301) 687-7740.

Aug 18–22. **Postgraduate Institute for Emergency and Primary Care Physicians.** Info: Office of Continuing Medical Education, University of California, San Diego School of Medicine, M-017, La Jolla, CA 92093. Tel: (619) 452-3940.

COLORADO

Aug 22. **Coding the Non-Acute Record.** Broadmoor Hotel. Info: CPHA—Insti-

(*Continued on p 11A*)



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NEW YORK STATE
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Efforts of the Medical Society of the State of New York to effect medical liability reform

DANIEL F. O'KEEFFE, MD

The medical malpractice situation in New York State has been a long-standing issue. The following statement from *News of New York* illustrates this point:

> "The malpractice crisis is not resolved, and remedial legislation at this session is urgent if we are to avoid a disaster in a few years. They point out that the current annual cost of medical malpractice insurance is almost $244,000,000 and predict that increases could rise to a half a billion dollars in three to four years."[1]

A key point of the statement is the $244 million cited as the direct annual cost of medical liability insurance. The direct cost has now been estimated to be slightly more than $700 million, with retroactive increases of as much as 40% to 55%.

In New York State, physicians have been struggling with the problem of medical liability for a long time. Some three years ago, the Medical Society of the State of New York (MSSNY) joined with other groups, insurers, specialty societies, hospitals, the New York Business Council, and the Chamber of Commerce to form the New York Medical Liability Reform Coalition. This group pushed hard for legislation that was introduced in both 1983 and 1984, but nothing passed. The Republicans in the Senate were sympathetic; however, the Democrats in the Assembly were not.

A crisis finally occurred in early 1985, when the State Insurance Superintendent announced the Gabrielli decision, which said that the Medical Malpractice Insurance Association (MMIA) should receive a 53% increase in premiums retroactive to July 1, 1984.[2] Other companies, the principal one being the physician-owned Medical Liability Mutual Insurance Company (MLMIC), were asked to file for increases based on the same criteria cited in the Gabrielli decision. The MLMIC filed for and was granted a 55% increase in their insurance premiums.

Faced with this increase, physicians rose up in force. In April 1985, some 3,000 to 5,000 physicians assembled on the Capitol lawn, protesting the high rates and demanding tort reform.[3] Governor Mario Cuomo came out with a bill that included voluntary and binding arbitration, structured awards, and reduced attorney fees. In the meantime, physicians, especially those in upstate areas, stopped doing certain high-risk procedures, and a major crisis evolved.

A watered-down version of the Governor's bill was passed by both Houses on the last day of the 1985 Legislature, and signed into law on July 2.[4] The Medical Society had opposed the bill as insufficient, but agreed it was a welcome first step after the Governor and Legislative leaders said they would work for a better solution in the fall.

The new law contains the following key provisions:

Increased malpractice prevention programs. The bill provides for the maintenance by each hospital in the state of a coordinated program for the identification and prevention of malpractice. This program includes the establishment of Quality Assurance Committees that would be charged with overseeing the hospital's malpractice prevention programs, ensuring the full exchange of information between hospitals concerning the granting of hospital privileges, and the establishment of educational programs and risk management plans to deal with patient safety and injury prevention.

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Address correspondence to Dr O'Keeffe, 45 Hudson Ave, Glens Falls, NY 12801.

Based on a presentation at the *Symposium on Medical Malpractice*, March 11, 1986, sponsored by the Department of Preventive Medicine and Community Health, State University of New York Health Science Center at Brooklyn.

Expert witness identification. The bill requires that full disclosure be made of the qualifications of any expert witness expected to be called by a party to a medical malpractice action along with the substance of that expert's testimony.

Pre-calendar conference and expedited discovery. The bill mandates the filing of a medical malpractice action with the court within 60 days after the issue is joined in the action, and would require that a pre-calendar conference be held in order to encourage settlement, simplify or limit issues, and establish a timetable for disclosure. The legislation also allows for expedited disclosure by providing for the completion of discovery proceedings no later than 12 months after notice of the action is filed. Finally, the measure requires that all parties be ready for trial no later than 18 months after notice of the action is filed.

Mandatory reduction of awards by future collateral sources. The bill provides that any award to a plaintiff in a medical malpractice action be reduced where the plaintiff's damages will, with reasonable certainty, be indemnified by collateral sources of insurance payable in the future.

Periodic payment of judgments. The bill provides for the periodic payment of judgments in medical malpractice actions. The immediate payment of any judgments for future damages would be limited to $250,000. Any judgments for future damages over that amount would be paid over the future period identified by the jury or court as the period during which it expects such damages to be experienced. In the case of pain and suffering, this period would be limited to a maximum of ten years. The security of such future payments is achieved by the entry of a judgment for the amount of the present value of an annuity contract sufficient to provide for future payments in periodic installments. On the death of a plaintiff, the liability for payment of any remaining installments of economic loss not yet due terminates except as to future earnings that will continue to be paid to the persons to whom the plaintiff owed a duty of support. These payments will continue for the remainder of the period originally found by the jury or until the duty of support ceases to exist, whichever occurs first. Any lawyers' fees allocable to that portion of the award payable in the future shall be reduced by calculating them on the basis of the present value of the annuity contract rather than the gross total of the payments to be made in the future.

Frivolous suits. The bill provides that if a party to a medical malpractice action either commences an action or interposes a frivolous defense, the court may award attorney's fees and court costs up to $10,000. These costs may be awarded not only against the party, but directly against his or her attorney as well.

Medical misconduct. The bill provides that any physician who has his or her license to practice medicine revoked or suspended in another state or who voluntarily surrenders his or her license after a disciplinary action in another state, may be brought up on misconduct charges in New York State. The measure also increases the triennial license fee by $90.00 and directs that such funds be used to improve the operation of the Office of Professional Medical Conduct.

Maintains medical malpractice panels. The bill maintains the current medical malpractice panels except in the Fifth Judicial District and the County of Suffolk where demonstration projects testing the effectiveness of the panels will be undertaken.

Reduces contingency fees. The bill reduces the contingent fees of lawyers in medical malpractice cases. Currently, attorneys are permitted to charge 33⅓% of the entire sum recovered. Under the new contingency fee schedule, plaintiffs' attorneys' fees are reduced as follows: From 33⅓% to 30% of the first $250,000; 25% of the next $250,000; 20% of the next $500,000; 15% of the next $250,000; and 10% of any further amount.

These reductions range from approximately 10% at the first level to a reduction in the attorney's fee of approximately 75% in the most severe cases.

Additional insurance coverage. The bill requires that every authorized medical malpractice insurer, including the MLMIC and MMIA, offer additional coverage of $1,000,000 over and above the $1,000,000/3,000,000 coverage presently offered. The bill further requires that such additional coverage must be purchased by every hospital in New York State on behalf of any physician who wishes such additional personal insurance protection if such physician "from time to time" provides emergency care in such hospital. The hospital is reimbursed for the cost of such coverage through increased reimbursement rates.

The effect of this provision is to provide the second $1,000,000/3,000,000 coverage at no expense to the physician, if he or she elects to accept it. The bill also guarantees the availability of insurance above the $2,000,000 level if a physician wishes to purchase that level of added protection.

Retroactive application. The bill is specifically made retroactive in most cases and its provisions generally apply to all actions that commenced after its July 1 effective date, regardless of when the alleged malpractice occurred.

Effect on premium. The bill specifically directs the Superintendent of Insurance to reassess the premium for the 1984 to 1985 premium year, and to take action to reduce the rate due to the retroactive application of the tort change in the bill. It is expected that the retroactive application of the bill will permit the Superintendent to reduce the increase effected by the Gabrielli decision by 45%, from 55% to 32%.

The bill also specifically requires the deferral of any new rate increase filing for the 1985 to 1986 premium year until the legislature returns to deal with the medical liability issue in the early fall.

What the bill did not contain were three major features that the Medical Society of the State of New York considered extremely important: a cap on pain and suffering at $250,000, voluntary and binding arbitration, and a limit of $1 million/$3 million on physicians' personal assets, with any excess over and above this to be paid for by the State. Also omitted from the bill were cases involving infants with birth defects and cases that were discovered four years after the occurrence.

Immediately following passage of the bill, an Ad Hoc Committee was appointed by the Medical Society of the State of New York, which consisted of representation from the nine district branches across the state, including the majority of specialty organizations, particularly those

that were of a high-risk nature (eg, obstetrics and gynecology, orthopedics, neurosurgery, family practice). This Committee met throughout the summer with Governor Cuomo's staff, as well as with the Senate and the Assembly, presenting proposals that could perhaps help to stem the tide of the malpractice crisis.

The next major development for medical liability was the release in mid-November of the Governor's long awaited follow-up proposal dealing with the medical liability insurance crisis.[5] The Governor's proposals were reviewed in detail by MSSNY's Council at its meeting on Thursday, November 14, 1985; after extensive discussion, the Council unanimously voted to disapprove legislation, terming it unacceptable.[6] The legislation proposed by the Governor in November contained the following provisions:

- A bill that would cap a physician's liability for all hospital-based malpractice incidents at $1 million. It is estimated that this absolute physician liability limit would apply to about 85% of the malpractice cases.
- The bill permits the inclusion of mandatory arbitration in Health Maintenance Organizations in enrollee contracts.
- The bill would extend the current premium freeze period to June 30, 1986.
- The bill would require that all policies issued in New York after July 1, 1986 be *claims made policies*.
- The bill provided that the physician discipline process would be shifted entirely to the Department of Health.

Representatives of the Medical Society of the State of New York held continuous meetings with the Governor's office, the Assembly, and the Senate. In response to the inadequacy of the Governor's proposal, the Senate's Republican Majority introduced a major medical liability proposal for consideration when the legislature returned to Albany in the fall of 1985. In this bill (Senate 6770, Lombardi et al), the following changes are included:

- A cap on pain and suffering at a level of $250,000.
- A system pursuant to which the future health care needs of a successful plaintiff would be paid for as such care was rendered (the so-called Federation of Jewish Philanthropy (FOJP) Proposal).
- A redefinition of the standard of proof necessary in a medical liability action so that a plaintiff would have to demonstrate his or her case by clear and convincing evidence.
- An amendment to the present law providing for the future payment of medical costs greater than $250,000, and to provide that where such projected damages existed, the entire amount of such damages would be paid in installments, not just the amounts greater than $250,000.
- Changes in the law governing damages so as to reduce damages for lost income to reflect the amount of taxes to be paid on such an award included in such damages because such taxes do not, in fact, have to be paid.
- Certain changes in the procedure law that would create a much broader right of discovery for the defendant in a medical liability case.

There was no second session. The New York State Senate passed the Medical Liability Reform Bill, which contained many of the Tort Reform concepts previously endorsed by the Medical Society of the State of New York. On the other hand, the New York State Assembly also passed a bill, Extraordinary Session A.1 Rules, at the request of the Governor. Since neither bill passed both Houses of the Legislature, no bill was enacted.[7] Immediately following the departure of the members of the legislature, the Medical Society of the State of New York entered into intensive negotiations with Governor Cuomo and the leaders of the Senate and the Assembly. I, as president of the Medical Society, along with our Governmental Affairs Officers, Mr Gerald L. Conway and Mr Jerry Hoffman, met immediately with the Governor's Secretary, as well as with members of the Assembly and the Senate. Meetings have been carried on continuously since. At this time (March 1986), the concepts currently under discussion include the following:

- A bill that would modify the present standard governing the Appellate Review of the size of a plaintiff's verdict in order to strengthen the power of the Appellate Courts.
- A bill that would require a reduction of an award to reflect the effect of Federal and State Income Taxes.
- A bill that would expand the use of arbitration in certain cases of conceded liability.
- A bill that would require a certificate of merit from a plaintiff's attorney before an action could be started.
- A bill that would contain a provision making the medical malpractice panels waivable by the defendant in certain cases.

It would seem that many physicians have adopted, up to now, a "wait-and-see attitude," holding in abeyance personal decisions about their practices that many of them thought they were forced to make last spring. Many physicians also thought on a personal basis, and not endorsed or encouraged in any manner by the Medical Society of the State of New York, that they would have to cease doing high-risk surgery. Obstetrical specialists contemplated dropping not only the high-risk obstetrical cases, but the practice of obstetrics entirely. Some physicians thought that they should retire early, while others considered giving their time to voluntary teaching assignments. In some cases, physicians decided to leave the state.

The implications for health care in New York State are profound. We are concerned, and must continue to fight for meaningful reform. It is an issue that affects all citizens, not just physicians in hospitals, and it affects society through the quality, availability, and cost of medical care.

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Medical liability: The perspective of the Medical Liability Mutual Insurance Company

DONALD J. FAGER, ESQ

A recent article in a professional journal bemoaned the dramatic increases in liability insurance premiums. Among the problems mentioned were an increase in the frequency and severity of claims, the litigious environment, the increased number of lawyers, litigation based on new theories of liability, and lawyers who have discovered malpractice as a lucrative practice specialty. Certainly, these comments will sound familiar to most physicians. The irony is that the article appeared in the *New York State Bar Association News* and it concerned the dramatic increase in insurance premiums for *lawyers*.[1] Perhaps at some point the members of the plaintiff's bar will tell us whether this problem is due to "bad lawyers."

It is astonishing indeed that medical liability premiums have now risen for the highest risk category in New York to more than $80,000 annually and that the premiums actually approached $100,000 before the Superintendent of Insurance required a 15% credit for the legislation that was approved in July 1985. Despite the obfuscation of those who would prefer to continue with the present system as it is, the major problem has been the dramatic and continuing escalation of claims costs. The million dollar verdict was unheard of until a few short years ago and it is now almost commonplace. Large verdicts do not even make newspaper headlines anymore unless they are of the multi-million dollar variety. The average cost of the disposition of cases rose from $36,000 in 1976 to $132,000 in 1984, and actuaries predict that incidents that occur in the July 1, 1985 to 1986 policy period will cost in excess of $500,000.[2] The simple reason for this is that our present system of compensating medical liability claimants is too costly, too time consuming, and is not really equitable. It takes an average of seven and a half to eight years to dispose of a case and, after all of the frustration and anxiety that litigants on both sides endure, we find that at least one half of the money goes to support the cost of litigation.

AN OVERVIEW OF RATES

As bad as the present insurance rates are, they have not for a number of years accurately reflected the gravity of the situation. In 1981, the Medical Liability Mutual Insurance Company (MLMIC) filed for a 52% rate increase and the Medical Malpractice Insurance Association (MMIA) filed for a rate increase in excess of 200%. The Superintendent retained an independent actuary who decided that the rate increase should be 107%. The Superintendent, however, then decided that the reduced birth rate would reduce the number of claims for babies with neurologic deficits and the practice of "defensive medicine" would help win more cases for the defense. Accordingly, he granted an increase of only 26%. In 1982, a request for a 71% increase was denied, with the Superintendent indicating that he would approve 15%. In 1983, a 50% increase was reduced to 25%. However, in 1981, the MMIA asked for and received a hearing on their request for a larger increase. A decision by a departmental hearing officer said that the MMIA should have had a 108% increase in 1981; however, it took several years, a new administration, and some pressure from the courts to bring that decision about. The current Superintendent then directed that a hearing be held on the 1983 and 1984 rates, and invited all of the carriers and the Trial Lawyers Association to participate. Every actuary who appeared at those hearings testified that the rates were seriously inadequate and the end result was a rate increase for the MMIA in excess of 50%, followed by a MLMIC increase of 55%.

It is important to note that the MLMIC, as a company owned and run by physicians, has a board membership composed almost entirely of physicians who pay these high premiums just like all of the other practicing physicians in New York State. It goes without saying that those physicians would not seek a rate increase unless they thought it was necessary. It also should be pointed out that unlike the commercial carriers, the MLMIC is not in the business to make a profit (in fact, the company was started in 1975 because the commercial carriers refused to write this volatile line of business any further), and uses every penny of investment income to keep the rates down. Further, it has a sound and conservative investment policy that has permitted it to rank among the top ten in the Best's Insurance Management Reports (the bible of the insurance industry) in return on the investment income.

MANAGEMENT CLAIMS

From the outset, the physicians who run the MLMIC decided that those claims that were groundless should be totally resisted and cases that were legitimate should be settled as rapidly and as equitably as possible. The MLMIC has taken a strong stand on groundless cases and thus far has closed about 57% of all lawsuits against its members without any indemnity payment. However, those cases cost money to defend and on a nonmonetary standpoint, the burden placed on physicians included in those cases is grossly unfair.

While cases of genuine malpractice should be settled early, recent large verdicts have so whetted the appetites of claimants and their lawyers that it has become increasingly difficult to settle those cases. The addition of an excess policy of $1 million for all physicians (purchased by

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their hospitals) will only exacerbate the already serious problem of large awards.

In the face of all this disastrous news, the plaintiff's Bar (with an enormous financial interest in the continuation of the present system) has taken the position that rate increases are not necessary because the MLMIC, among others, has an enormous asset base in excess of $1 billion. That charge belies the historical record of this "long tail" malpractice business. A look at the experience of Employers Insurance of Wausau, the carrier for the State Medical Society program for 25 years, is illustrative. In 1973, the last year Employers wrote medical liability insurance in New York, they collected a premium of approximately $36 million dollars and paid out about $1 million dollars. Those who were involved at that time will recall that the plaintiff's Bar accused Employers of leaving the business having made copious amounts of money. The fact of the matter is that although Employers has not written a professional liabilty policy in New York for more than 12 years, they have, in the last five years alone, paid out more than $180 million in losses. A recent actuarial estimate indicates that Employers will lose about one half billion dollars on Medical Society business. The early years of the MLMIC's experience tell virtually the same story. In 1975, the company collected $68 million in premiums. To date more than $95 million has been paid and there are reserves on known cases exceeding $70 million. This does not even include the so-called incurred but not reported cases (IBNR) and each month the company receives new claims dating back to policy year 1975. In policy year 1976, $84 million was collected in premiums; to date $92 million has been paid in losses and reserves exceed $94 million on *known* claims. The real issue is not whether the MLMIC has too much money but whether it will have enough money to pay all of the claims in the future.

Loss Prevention Effort

The physicians who run the MLMIC feel a keen responsibility to do everything in their power to reduce losses. From the outset, physicians have been involved in alerting their colleagues to problems that arise in claims and offering advice with respect to patient rapport and communication, record keeping, and consultations. This program has become even more encompassing in the Hospital/Voluntary Attending Physicians Program wherein the MLMIC not only lectures to physicians, residents, and nurses but is involved in the hospital's quality assurance mechanisms in an effort to reduce losses. Some 24 hospitals in the state are enrolled in the program with physicians whose primary affiliation is at those hospitals, and receive a discount from the regular premiums of 25%. The program is designed not only to be a more effective tool in risk management but to bring together the hospital and the physician as natural allies in defense of the cases, rather than having them working against each other to the benefit of the plaintiff.

The loss prevention plan of the MLMIC also involves careful monitoring of the methods of practice and loss experience of insured physicians. Those with adverse loss experience are interviewed by their peers. However, physicians are not penalized merely because they have claims asserted against them or in fact merely because claims have been paid. Recommendations that insurance coverage be canceled or restricted are not lightly made and only after the peer review group (the Professional Medical Liability Insurance Board of the State Medical Society or the Claims Committee of the company) has made a determination that the physician's claim record is due to methods of practice that fall below acceptable standards.

Merit Rating Plan

Following legislation in July 1985, the insurance department of the MLMIC proposed that physicians be surcharged according to a merit rating plan that will assign points and surcharges according to a rigid formula based upon paid claims. Both the MLMIC and the Medical Society of the State of New York strenuously objected to this approach and the company has filed an alternative merit rating plan that will allow physicians to be reviewed through a peer review mechanism much as it presently does, with the number of claims and loss payments serving only as a mechanism for identifying physicians for review. The plan has been endorsed by the House of Delegates of the Medical Society of the State of New York.

While the MLMIC is working diligently in all of the areas discussed herein, physicians still cannot anticipate relief from the intolerable burden of medical liability premiums without a fundamental change in the present system of compensating medical liability claimants. When the MLMIC was formed in 1975, physicians said then that it would not solve the problem without dramatic changes in the tort liability insurance system. Sadly, those changes have not yet taken place.

References

1. "Lawyers facing professional liability bind." New York State Bar Association *News* 1985; 27(7):1.
2. Report of the acturial firm Millerman and Robinson, in conjunction with Medical Liability Mutual Insurance Company rate filing, 1986.

Medical malpractice as seen from the perspective of the physician's defense attorney

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The view of the defense counsel in representing physicians in malpractice suits is probably very narrow, if not myopic. Nevertheless, lawyers may have some insights as to forces that are affecting the ultimate factors in the medical malpractice crisis (ie, the outcome in the courtroom). The reason that there is a crisis is because something seems to be going wrong in the disposition of trials, particularly with the amount of damages being awarded. It may be of some comfort to know that physicians are not alone in feeling overwhelmed by this problem. Over the last three years the professional liability insurance for our firm, which has never made a claim, has gone up 953%. This indicates that attorneys are catching up to physicians in the crisis.

There is a continuing myth that physicians win 85% to 90% of the cases that are tried and, therefore, there should be no need for concern. No one has ever cited what authority is being referred to with these statistics, and the only viable statistics around suggest that nothing could be further from the truth. The *New York Jury Verdict Reporter*,[1] which is a journal designed to summarize verdicts of all kinds in New York State, has published solid statistics. These data show that in the trial year 1981 to 1982, the plaintiffs won 30% of the malpractice cases that were tried to a conclusion. In the trial year 1982 to 1983 the plaintiffs won 41% of the cases, and in trial year 1983 to 1984, the plaintiffs won 43% of cases.

The Jury Verdict Reporter does not account for every malpractice case tried in the state, but the numbers are large enough that the statistics and averages are probably accurate. In fact, these statistics are misleading because they do not take into account all of the cases that have been settled prior to or during a trial. Consequently, the figures are much bleaker than they appear on the surface. The cases that are being taken to conclusion are those that the physicians and insurance companies believe they should win. If they did not think they had a good chance of winning, the case would most likely be settled. Consequently, it appears that the trend in the near future is that defendants in malpractice cases will have no better than a 50% chance of winning the cases that by medical standards are defensible.

AMOUNT OF AWARDS

The issue of the amount of awards seems to be even worse than the issue of winning or losing a case. Using the same set of cases over the same period of time, the *New York Jury Verdict Reporter* states that the average award in a medical malpractice case in the year 1981 to 1982 was $542,000. For the year 1982 to 1983, the amount was $1,893,000. In the year 1983 to 1984, the amount dropped to $966,000. Clearly the enormous increase from 1982 to 1983 cannot be accounted for by inflation or by any other rational explanation. The fact that there was a decline to roughly $1,000,000 in the year 1983 to 1984 is not reassuring.

It should be noted that these numbers reflect what the jury awarded and do not take into account those awards that may have been reduced or even eliminated by an appeal. What they do show, however, is that there are hostile forces at work in the courtroom. Although this may appear to be an attack on the jury system, that is not the case. A great deal of confidence may be placed in a jury system wherein the jury is truly composed of a cross section of the community; the jury has the opportunity to listen to a case that is presented based on the rules of evidence; and the jury receives an appropriate charge from the court. However, that combination seems to come together quite infrequently.

The defense counsel has the responsibility to advise their client as to the likelihood of the outcome of a trial; not only winning and losing, but also the estimates as to what amounts would be appropriate for a settlement of a jury verdict. Historically, the counsel has been able to exercise judgment in a way that generally gave the clients a reasonably good estimate as to their exposure. Based on the above average awards, however, where accurate assessments may have been given prior to the year 1981 to 1982, those same estimates would have been grossly inaccurate for the year 1982 to 1983. By the very nature of the process, counsels' estimates as to the prognosis have become less and less accurate.

BILL OF PARTICULARS

The defense counsel attempts to evaluate the case very soon after it has begun. This evaluation should start with an analysis of a Bill of Particulars, which the plaintiff is required to serve in response to a demand by the defendant. That document is a clear statement of the allegations of negligence and damages. However, this document has become less and less one of particulars and more a statement of generalities that gives virtually no information as to what the claim may be.

Obstetrical cases provide the best example of a Bill of Particulars, by stating the following: the prenatal care was negligent; the delivery was negligent; the postnatal care was negligent; the patient should not have received pitocin; a cesarean section should have been done; or if it was done, the surgery should have been done earlier. This ritu-

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alistic Bill of Particulars gives no information on which one may make a judgment.[2]

Will this inequity be cured by the new legislation that was passed in June of 1985?[3] The new legislation includes a section that requires the plaintiff and defendant to exchange expert's reports that should include the basis of the expert's opinion. Although a quick reading of that statute implies that there will be an exchange of opinions, there are, in fact, several caveats. To begin with, if the plaintiff can show that they have not retained an expert before trial to exchange an opinion or report, they are in no way precluded from introducing an expert's testimony at trial. Consequently, the statute favors the plaintiff not getting the case reviewed until just before trial and then not exchanging the opinion. There is a specific additional exemption in a medical malpractice case. In a medical malpractice case, as opposed to all other negligence cases, the party exchanging the report is not obligated to give the name of the expert who has given the opinion.

Expert Witnesses

Federal rules have required for many years that not only will the names of experts and the essence of their testimony be revealed, but, if requested, the opposing side may actually take their deposition before the trial. This process is not limited to the federal courts, and, in fact, is a common practice in most states.

It does not take much reflection to appreciate the intelligence of this type of rule. Both sides are clearly on notice as to the other party's case. Rational decisions may be made long before the trial as to whether this case is one that really should be tried, settled, or discontinued. However, that does not mean that everyone gives up on the trial; rather, rational decisions are being made. It appears that the fundamental reason for keeping discovery to a minimum is that New York is intent on preserving the hallowed tradition of trial by ambush.

Information from Subsequent Treating Physicians

In the past, common practice dictated that the first element of investigation was an interview with the subsequent treating physicians. Although the reasoning is almost simplistic, it was tremendously helpful. Within a short time, it was made clear whether the subsequent treating physicians either confirmed the injury that was being claimed, or would take a position that the plaintiff was fabricating the injury. Equally important was the benefit of an immediate review of the defendant's treatment. The subsequent treating physicians were in an excellent position to give an indication as to whether the prior treating physician, the defendant, adhered to acceptable practice. Often candid and helpful commentary was provided by the subsequent treating physician. In general, the result of these interviews provided information from which it was possible to make an accurate analysis of the case concerning both liability and damages. This also led to a reasonable position on the defendant's part as to how the case should be disposed. That is, if the defendant was clearly in trouble, the case would then be settled. The converse was equally true. However, this was all changed by a decision of a judge in Queens in the case of *Anker v Brodnitz*.[4]

In the past, the Court of Appeals[5] determined that when a litigant brought a case involving an issue of the plaintiff's physical condition, the plaintiff automatically waived any right of confidential relation between physician and patient. There was a simple logic involved: if the plaintiff was suing because of an alleged injury, the defendant had every right to search out all of the medical treatment and all of the physicians that might possibly be involved to either corroborate or undo the plaintiff's position. Obviously, in a medical malpractice case, the plaintiff's physical condition is invariably an issue. Nevertheless, with the *Anker v Brodnitz* decision, and its approval by an appellate court, a large part of the state of New York now prohibits the defense in a medical malpractice case from speaking to any of the subsequent treating physicians. However, the defense is permitted to obtain a copy of the medical records the physician may have although they may not ask for an interpretation of the records, for a clarification of the records, nor for any conversations that may have taken place with the patient. There may be no communication. This exclusion is limited to malpractice cases. If a plaintiff is suing because of an automobile injury, the defendant in that case may interview all the physicians that he chooses.

Consequently, the defense, with the constrictions that are growing, is placed in a more difficult position in defending these cases than had been years ago. It is much more difficult to give a realistic appraisal of potential liability and damages. It appears now to be much more of a guessing game. One often hears the expression that a trial is "the search for the truth." However, nothing could be further from the truth.

Issue of Damages

In common law (and in theory all legal concepts have been derived from common law), an action for wrongful death did not exist. The concept was that if someone died as the victim of negligence, his right of action died with him. As the public became more enlightened, statutes were passed that permitted specific limited recoveries for wrongful death.

The modern statute may be found in the Estate Law of New York; those rules specifically limit the award for damages in an action for wrongful death to the "pecuniary injuries" to the person for whose benefit the action is brought.[6] Initially, the term "pecuniary," which by definition means measured by money, was limited to prospective dollars in terms of earned income that would be lost because of the death of the individual. Consequently, one could project rather easily the recovery for the wrongful death aspect of a case. If a wage earner had an income of X and a prospective work life of Y, a simple $X \times Y$ would approximately equal the loss.

In recent years, the judiciary has determined that the term "pecuniary" has a much broader definition. It now includes not only lost income but also loss of support, loss of services, loss of voluntary assistance, loss of prospective inheritance, and something which is impossible to value, the loss of parental guidance for minor children. The point is that in spite of the specific limitation in the statute, the

judiciary has systematically expanded the damages for wrongful death.

It should be made known that in most cases, if the plaintiff wins, he is entitled to interest on the award from the date of the judgment. In wrongful death, if the plaintiff is successful, he or she collects interest from the date of death. Consequently, allowing an action for wrongful death to linger inures to the plaintiff's benefit. As the years of interest continue to build, the potential verdict becomes larger due to the accumulating potential interest.

There is no end to the creativity of the judiciary. In a recent case in which the plaintiff has been in a coma for years and will remain in a coma until death, the jury was given a verdict sheet for damages that included a place for loss of past earnings, loss of future earnings, pension loss, future hospital expenses, future nursing care, conscious pain and suffering, and a new entry: loss of enjoyment of life.

One must wonder at the comments from the chief judge of the Supreme Court of the United States, who bemoans the enormous number of cases that are being brought in federal and state courts. It is amazing that it has not occurred to that judge that the attraction of the litigation process has been enhanced many times by the judiciary. It is the judiciary that has encouraged lawsuits, has raised the stakes of lawsuits, and, to some degree, has made the whole process into a lottery. Some have forgotten that the judge is to be the ultimate umpire, not a player. However, this is not always the case; in most instances the law, both procedurally and substantively, is applied with knowledge and fairness.

Joint and Several Liability

Nevertheless the judicial lottery exists, and a rather sophisticated part of the lottery element is the result of an old common law concept that is described as "joint and several liability." The concept is that any defendant who is found responsible for an injury is responsible for 100% of the damages. That does not mean that each defendant must pay 100%. The plaintiff still may only collect 100% of the verdict or award. The sophisticated part comes into play when there is more than one defendant, and the lesser involved defendant has more assets (coverage) and is designated the "deep pocket." For example, in the classic obstetrical case, the obstetrician is obviously the main target. The plaintiff may assume that he already has that doctor's policy. The game, and it can be referred to as the 1% game, is to try and hold someone who really has no liability in the case for at least 1% of the liability. In the example given here, it could be the anesthesiologist or the hospital itself, who may really have had no involvement in the delivery. The point is, if the plaintiff can get a multimillion dollar award and get several defendants in for very small percentages, he can collect up to the full amount of coverage from each defendant. The point is that if a defendant is held in for 1%, he does not necessarily pay 1%. Rather the defendant pays whatever the plaintiff can get from him, and that may be his entire policy.

In a recent trial, the primary defendant, a surgeon who had a $1 million malpractice insurance policy, was found to be 80% responsible for an injury. The referring physician, who had a $2 million policy, was held to be only 20% responsible. The total verdict was $3 million. If the verdict is not reduced by the court, the referring physician is not limited to $600,000 (20% of $3 million); the plaintiff may collect the entire amount above the surgeon's policy (ie, $2 million). The result would be the same if the referring physician had been held to be 1% responsible. Although it seems patently unfair that a defendant who is held to be 1% responsible may be responsible for the entire judgment, that is the present state of the law.

Damage Elements and Itemized Verdicts

A few years ago, legislation was passed that mandated that a verdict in a medical malpractice case must specifically itemize the damage elements. That is, the jury must specifically say how much was awarded for such items as pain and suffering, past medical expenses, and lost earnings. It has never been clear exactly what that legislation was intended to achieve. Nevertheless, there has been a byproduct of the legislation that was totally unintended and is very detrimental. The courts have not only requested itemized verdicts as to damages, but also itemized verdicts as to the issues of liability. That is, at the close of the case, the courts routinely give the jury a list of the claims that are being made by the plaintiff. It is not unusual for a jury to receive from one to eight or nine different theories of potential liability. The net effect is that the defendant must win on each of the issues in order for there to be a defendant's verdict, while the plaintiff need win on only one to have a plaintiff's verdict. Consequently, the burden of proof has been shifted from the plaintiff to the defendant.

Traditionally, the entire case went to the jury, and the plaintiff had the burden of proving the theories he presented during the trial. The jury returned a single verdict on the issue of liability; either they found malpractice or they did not. The jury was not asked to identify which theory or theories they accepted. If the plaintiff prevailed on the general verdict, he faced the possibility of an appeal if his proof on any issue he sent to the jury was insufficient as a matter of law. Consequently, the burden was on the plaintiff to delimit the proof and the theories that went to the jury.

Under the developing procedures of the itemized verdicts, the plaintiff now is free to use a shotgun approach in the hopes that the jury will be satisfied on any theory. There is now no risk to the plaintiff to invent as many theories as he chooses. Consequently, the entire concept of itemized verdicts works to the detriment of the defendant.

Conclusions

Physicians must understand that what has been described is a hostile environment. Many jurors are clearly unhappy with their relationship with the medical community. It is often the case that jurors and patients have unrealistic expectations as to what may be accomplished with medical treatment. To a large degree this is a product of the medical community's inappropriate public relations. In addition, potential jurors often excuse themselves because they feel they have had unfavorable experiences with the medical community. The level of sophistication

of the patient has been raised to unprecedented levels. That sophistication must be met with intelligent communication and caring attitudes. The medical community must remember that what it considers routine treatment is in all likelihood strange and terrifying to the patient.

The liability crisis is not limited to physicians. However, physicians must seriously examine what they can do to reduce the level of suspicion and unhappiness on the part of patients. The patients who become jurors currently show little sympathy for physicians.

The above discussion does not touch all of the corrections the defense counsel would recommend. Consequently, in the event physicians seek further changes in the legislation that controls the tort system, it might be useful for them to discuss the issues with their attorneys. They might have something useful to say.

References

1. *The New York Jury Verdict Reporter*, Cumulative Index and Statistical Survey for Volume 111, Metropolitan Edition, covering the five counties of New York City, Nassau County, Suffolk County, Westchester County, Southern District of New York, and the Eastern District of New York.
2. *Cirelli v Victory Memorial Hospital*, 45 App. Div. 2d 856 (2nd Dept. 1974).
3. In a case presently being tried (not subject to the new legislation) in Queens, the plaintiff has been allowed, after selection of the jury, to amend the bill of particulars to change the date and place of the alleged malpractice.
4. *Anker v Brodnitz*, 73 App. Div. 2d 589 (2nd Dept. 1979).
5. "We hold, therefore, that by bringing . . . a personal injury action in which mental or physical condition is affirmatively put in issue, a party *waives* the privilege." 25 N.Y. 2d 287 (1969) at 294.
6. EPTL § 5-4.3 specifically includes in addition to "pecuniary injuries": medical expenses and funeral expenses.

1987 Albion O. Bernstein, MD Award

The Medical Society of the State of New York is accepting nominations for the 1987 Albion O. Bernstein, MD Award until October 1, 1986.

This national award is given to a physician or scientist who has made a significant contribution in medicine or surgery. Recent winners include Drs Baruch Blumberg, Lawrence Hinkle, and Stanley Dudrick.

The $2,000 award and appropriate scroll will be presented at the Annual Meeting of the Medical Society of the State of New York, March 12–15, 1987. The award was endowed by the late Morris J. Bernstein, MD in memory of his son, a physician who died in an accident while answering a hospital call in November 1940.

Nominators must complete and submit the official nomination form with additional support information which must include the nominee's curriculum vitae, a brief synopsis of the significance of the achievement, a list of publications, and a personal letter(s) of recommendation. Please submit by October 1, 1986.

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Medical malpractice: The patient's point of view

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In the present "malpractice crisis," physicians are convinced that lawyers are responsible for their dilemma. Maybe they are and maybe they are not. Lawyers think that the villains are actually the insurance companies, especially the physicians' own company in New York. The Medical Liability Mutual Insurance Company presently has assets of about $1.5 billion, and in the ten years it has been in existence has never paid out one dollar of the millions of dollars in premiums it has collected from physicians. All of its payments have been from investment income, which is more than $100 million per year. In any event, it is not the purpose of this article to engage in the polemics of who is right and who is wrong, but rather to deal with the circumstances that expose a physician or hospital to liability, as seen through the eyes of a patient's lawyer.

PHYSICIAN LIABILITY

One of the statements I have often heard physicians make is that there is no *definition* of what is medical malpractice, and that it is a vague, amorphous thing left for the jury to decide. This is a misconception. The term is clearly defined, and by legal definition is "bad or unskilled practice on the part of a physician that causes harm to the patient." It is its application to a given set of circumstances that results in divergent opinions.

There are three essential elements that a plaintiff must prove to establish a prima facie case of malpractice: (1) The relationship of physician and patient. (2) That there was a departure from a duty owed by the physician to the patient. (3) That the departure caused or contributed to the injuries or complications of the patient (ie, was its "proximate cause").

The relationship between physician and patient is usually the result of a voluntary agreement between the two individuals. The conduct of the parties determines the relationship. Ordinarily very few formal words are exchanged. Even the matter of the fee is often not discussed. The relationship is not altered even if there is no fee involved.

A physician is under no duty to render his or her services to anyone, and is not liable for the consequences of such a failure to treat, unless the physician is connected with a governmental agency or a hospital that has a specific duty to the members of the public.

The physician and patient relationship, which imposes a duty to use care, may arise when the services of the physician have been obtained for the patient's benefit, even though the patient did not personally hire the physician. The relationship may also be created by an agreement between the physician and a third person who is not the patient. Indeed, the relationship may arise merely from a telephone conversation. For example, a man who had a heart attack came to the emergency room of the defendant hospital in the early hours of the morning accompanied by his wife. The nurse in charge was told about the heart attack and treatment was requested. The man mentioned that he was a member of the Health Insurance Plan (HIP). The nurse replied that the hospital could not take care of patients of HIP, but would try to get a physician affiliated with the plan. She telephoned the codefendant, Dr X, and explained the facts to him. The man then took the telephone and described his pains to Dr X. When the conversation ended, the man informed the nurse that the physician had told him to go home and to return when the HIP office was open. The man once again asked the nurse to get a physician because this was an emergency, but the nurse refused and said that the patient would have to see his own private physician. The man then returned to his apartment, and, while undressing, fell to the floor and died.

The physician's version of the telephone conversation was that he offered to come to the emergency room and examine the man, but that the latter declined, stating that he felt better and would prefer to see another physician.

The trial court dismissed the case, but the appellate court reversed the dismissal as to both the physician and the hospital. It ordered a new trial and stated the following[1]: "We must hold that the jury could have concluded that Dr X undertook to diagnose the ailments of the deceased and could have decided whether he abandoned the patient, inadequately or improperly advised him, or conversely, made a proper diagnosis fully appropriate under the circumstances, or offered an examination which was rejected."

As to the departure from a duty owed by the physician to the patient, a leading case, *Pike v Honsinger*,[2] which dates back to 1898, laid down the rule that a physician basically owes five obligations to a patient: (1) "[The physician possesses] that reasonable degree of learning and skill that is ordinarily possessed by physicians and sur-

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geons in the locality where he practices . . . ." (2) "[The physician is] to use reasonable care and diligence in the exercise of his skill and the application of his learning to accomplish the purpose for which he was employed." (3) "[The physician is] to use his best judgment in exercising his skill and applying his knowledge." (4) "[H]e is bound to keep abreast of the times." (5) "[A] departure from approved methods in general use, if it injures the patient, will render him liable however good his intentions may have been."

Proof that a physician was guilty of a departure from accepted standards of medical practice is not enough to determine malpractice. The patient may have already been suffering from an injury, disability, or pain. The patient must then prove that the malpractice on the part of the physician caused, precipitated, or hastened the condition. For example, a plaintiff sustained fractures of his left tibia and fibula in a fall. The defendant immobilized the fractures in a plaster of Paris cast; however, because the cast was applied too tightly, a disturbance in circulation occurred and the plaintiff developed a thrombophlebitis of the leg. For the plaintiff to prevail, he would not only have to prove that there had been a departure from accepted medical practice in the way that the cast was applied, but also that it was the proximate or contributing cause of the injury for which he sought damages.

Breach of Contract

A physician may also be liable to a patient for breach of contract where he or she agrees to effect a cure or a specific result. This becomes a *contract* action, rather than one in tort. However, the courts view with disfavor an attempt by the plaintiff to plead a contract action (because it has a longer statute of limitations), in a case that is essentially a malpractice action.

A physician and patient are always at liberty to contract for a particular result. Where a physician promises to effect a cure or to produce a specific therapeutic result, in addition to performing in accordance with the applicable standard of care, contract principles will govern. In such cases, the physician has promised to do more than is required of him by law and can be liable for breach of contract even though he used the highest professional skill.

In the case of *Robins v Firestone*,[3] the plaintiff claimed that he employed the defendant, a physician, for a fee to perform an operative procedure for the removal of polyps on the bladder. He alleged that "defendant agreed, as his part of the contract, to perform the operation in a good and workmanlike manner and promised to cure the plaintiff," but failed to do so. The statute of limitations (which then in New York was three years for malpractice and six years for breach of contract) had already expired for malpractice, so that the complaint could only stand if it stated a cause of action for breach of contract. The appellate court held that it would be an error to dismiss the complaint, because it properly stated a cause of action for breach of contract.

It has also been held that a cause of action for breach of contract was stated (and thus not barred by the statute of limitations for malpractice) where the plaintiff claimed that the defendant had contracted to perform an operation known as a "Cauldwell-Luc" on him when in fact, that type of operation was not done, and, in any event, the operation was done in whole or part by a surgeon other than the defendant.

If the plaintiff originally sued for malpractice, and the complaint at trial was dismissed because the plaintiff failed to prove a cause of action, this would not preclude a subsequent action for breach of contract. These are two different causes of action, although they both arise out of the same transaction. The dismissal of one is no bar to the other. Furthermore, in an action for breach of contract, expert testimony to prove the breach is not necessary.

The rule of damages in an action for breach of contract is somewhat different from that of a malpractice case because pain and suffering is ordinarily not an element.

Corpus Juris Secundum[4] states the rules: "The damages recoverable for a breach of contract to use reasonable care and skill in treating a patient are such as naturally flow from the breach. Where the contract was for a particular result, damages are limited to payments made to the patient, and the patient's expenditures for nurses and medicine or other damages flowing from the breach of contract. The damages for breach of contract to cure are the difference between the value of the condition promised and the actual condition, including incidental consequences fairly subject to the contemplation of the parties when the contract was made; but the patient cannot recover as damages for breach of contract to cure, suffering incident to the treatment or for excess of suffering from treatment over that promised. Where the services are performed in a manner different from that expressly agreed to, damages may be recovered for pain and disfiguring as a result. Damages for mental anguish have been allowed where physical pain resulted from a breach of contract to treat a patient."

Liability of a Hospital

Although a charitable-immunity rule still exists for hospitals in some jurisdictions, the prevailing trend is to abolish this immunity. In states that have abolished the immunity rule, hospitals are now governed by the general doctrine of *respondeat superior*, insofar as liability for torts of employees and agents of charitable corporations is concerned.

In New York State, a hospital is liable for the medical or administrative acts of its employees (ie, residents, interns, nurses, orderlies), but generally not for the negligence of an attending physician. The latter is usually not an employee of the hospital. A hospital is liable for the acts of an attending physician if it is a municipal hospital where, by special statute, the municipality has assumed responsibility.

A hospital may also be found liable if it negligently allows an unqualified physician to operate therein (ie, gives a physician privileges without adequately checking references and qualifications). Several cases have noted that hospitals may be found liable if they fail to monitor the abilities of attending physicians who operate there. If a particular attending physician is sued over a course of time by several patients, and the hospital does nothing to investigate his or her qualifications, the hospital may be found liable.

In the case of *Bing v Thunig*,[5] in applying the rule of *respondeat superior* and overruling an earlier decision that had established the principle that physicians, nurses, and even orderlies, when performing "medical" acts, were independent contractors for whom the hospital was not liable, the New York Court of Appeals used the following language:

> "The conception that the hospital does not undertake to treat the patient, does not undertake to act through its doctors and nurses, but undertakes instead simply to procure them to act upon their own responsibility, no longer reflects the fact. Present-day hospitals, as their manner of operation plainly demonstrates, do far more than furnish facilities for treatment. They regularly employ on a salary basis a large staff of physicians, nurses and interns, as well as administrative and manual workers, and they charge patients for medical care and treatment, collecting for such services, if necessary, by legal action. Certainly, the person who avails himself of hospital facilities expects that the hospital will attempt to cure him, not that its nurses or other employees will act on their own responsibility."

Hospitals should, in short, assume the responsibilities borne by everybody else. There is no reason to continue their exemption from the universal rule of *respondeat superior*. The test should be for these institutions, whether charitable or profit-making, as it is for every other employer: was the person who committed the negligent injury-producing act one of its employees and, if he was, was he acting within the scope of his employment?

A hospital will also be liable under the doctrine of *respondeat superior* for the acts of its "specialists," such as anesthesiologists, radiologists, and pathologists if they are employees of the hospital. If they are not employees but rather operate under some concession arrangements or enjoy a monopoly of a particular department in a hospital, the hospital may still be liable for their negligence.

In the case of *Seneris v Haas*,[6] the court stated the following:

> "Plaintiffs here through the questions permitted them showed the defendant West was one of six anesthetists on defendant hospital's panel, or staff; that he gave anesthetics for no other hospital; that he had regular on call duty at said hospital; that a hospital nurse summoned him to give the anesthetic in question. It appears that this evidence is sufficient to establish, prima facie, that defendant West was an agent of defendant hospital. There is nothing in the record to show that plaintiff should have been on notice that defendant West was not an employee of defendant hospital and it can not be seriously contended that she was obliged to inquire whether each person who attended her in said hospital was an employee or an independent contractor. It follows that the trial court erred in taking the issue of agency from the jury."

In the case of *Hryniak v Nathan Littauer Hospital*,[7] the court held that a hospital does not have a duty to preserve radiographs of a patient. In the case of *Fox v Cohen*,[8] the court held that a duty to preserve hospital records exists. Should the patient lose a malpractice suit because of a loss of records, a valid cause of action exists against the hospital for damages suffered by reason of the loss.

Hospitals have also been held liable for the following reasons.

1. Failure to admit a patient when they should have.
2. Prematurely discharging a patient or improperly moving the patient from one hospital to another when this resulted in the patient's death.
3. Failure to exercise "reasonable care in the selection and maintenance of equipment and facilities furnished" to the patient.
4. Failure to properly supervise a patient who is in the delivery room and becomes mentally deranged (intrapartum psychosis) or who has shown evidence of mental instability.
5. Giving the patient mismatched blood or other improper medication.
6. Permitting a patient to be burned with a hot-water bottle, heat lamp, or similar device.
7. Failure of a resident at hospital to notify promptly the treating doctor of "significant adverse change" in the patient's condition.
8. Injection by nurse of tetanus toxoid with resultant paralysis of arm, where proof was that it was given too low and thus injured the axillary nerve.
9. Failure to perform a proper "cutdown" for insertion of a needle for intravenous fluids.
10. Failure to provide a sufficient number of nurses trained to recognize the progressive gangrene of a patient's leg and also for the failure to require consultation with, or examination by, members of the hospital staff as required by the hospital's own rules.
11. A hospital is obliged to carry out the physician's orders and cannot substitute its own ideas even though by doing so it is following customary practice.
12. Failure to provide adequate personnel to assist elderly patients to the bathroom.
13. A hospital is liable for illegal treatment given to a patient with the knowledge of the hospital administrator.
14. A hospital may also be found liable, as any property owner, for general acts of negligence dealing with the property owner's obligation to maintain and repair the premises.
15. A hospital also has an obligation to maintain medical records. If this is not done properly and thoroughly to the detriment of the patient in a subsequent action, a separate action will lie against the hospital for this impropriety.

Statute of Limitations

In New York State, the statute of limitations is 2½ years for a medical malpractice action for injuries and two years for wrongful death. A cause of action against a physician predicated on lack of informed consent is governed by the 2½-year statute of limitations rather than the one-year statute for a battery stemming from the unconsented touching of the body of the patient, since the physician's failure to supply the patient with necessary information constitutes an act of malpractice rather than a battery. A plaintiff who sues the physician for damages for breach of contract (arguing that the defendant expressly or implicitly contracted to achieve a given result) would get the benefit of a longer six-year statute of limitations. In such instances the court would look through the complaint to see the substance of the allegations contained therein. If the substance of the action was malpractice and not breach of contract, the shorter 2½-year statute would apply.

In an action for damages for injuries suffered as a result of medical malpractice in New York State, the statute of limitations period commences running from the date of the wrongful treatment. This is true even if the plaintiff does not know of an injury or of the impropriety of the treatment. In this regard New York espouses the minority view. Most jurisdictions apply the so-called discovery rule, which states that the limitation period commences running when the patient knows, or in the exercise of good judgment should know, that he has suffered an injury as a result of a medically-related act.

In New York, there are two exceptions to the general rule concerning accrual of the cause of action for purposes of the statute of limitations. These are the *foreign object* and *continuous treatment* exceptions.

When a foreign object has negligently been left in the patient's body, the limitation period will not begin to run until the patient could have reasonably discovered the malpractice. In such a case, the period is one year from the date of discovery or 2½ years from the date of the malpractice (operation), whichever is later.

That the defendant knew he or she left a foreign substance in the patient and had failed to inform the patient may be the basis of a fraud action. When the defendant has left a foreign object in a patient's body and continued treatment without disclosing this fact or treating the plaintiff for the foreign object, it has been held to constitute continuing negligence in treatment. The statute of limitations will not commence running until the termination of the treatment.

Indeed, when there is a continuing course of treatment and the injuries occur in the course thereof, the statute does not begin to run until the termination of the treatment. Whether or not treatment is "continuous" is a question of law to be decided by the court. If the period of time between two treatments is greater than the statute of limitations (2½ years), then the treatment will be held, as a matter of law, not to be "continuous." With this minor exception, the cases usually are difficult to decide and depend on such factors as frequency of visits, treatment rendered during the visits, states of mind of the patient and physician, and telephone calls made to or by the physician.

An action against a hospital, if predicated not on the acts of a physician or surgeon but only on the acts of nurses (nonmedical acts) or administrative employees, is not a malpractice action. Rather it is a negligence action and gets the benefit of the longer (three-year) statute of limitations.

The statute of limitations may be tolled for infancy or insanity, but not by reason of the defendant's absence from the state, provided that the action accrued in New York. The extent of the tolling depends on whether the cause of action accrued before or after July 1, 1975. If a child was injured at birth as a result of medical malpractice on June 30, 1975, that infant has eighteen years plus 2½ years within which to commence an action. If that same child was born on July 1, 1975, the statute of limitations is ten years.

Finally, a physician should always remember Hippocrates' admonition:

1. To try to make the patient better.
2. If you cannot make him better, try not to make him any worse.

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The industrial perspective on medical malpractice

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Until recently, industry paid relatively little attention to the medical malpractice problem, or the malpractice crisis as many have called it. It was viewed largely as a struggle in which physicians, health professionals, and hospitals clamored for reform of the tort laws that would lower their costs by controlling the number of claims and the size of awards while lawyers, especially those of the plaintiffs, successfully fought for the most part against any curtailment of their prerogatives. Malpractice carriers were regarded both as victims and villains: the former because of the increasing burden of defending claims and the rising costs of the awards they had to pay when the defense was unsuccessful or had to be settled, and the latter because of their rapidly rising premium rates. While these views persist in many quarters, the last five years have seen a growing awareness and concern on the part of industry that both reflects and is reflected in the activities of health action coalitions like the New York Business Group on Health.

The New York Business Group on Health is a not-for-profit coalition of almost 300 employers in the New York City metropolitan area, comprising large and small businesses; insurance carriers; consulting, law, and accounting firms; labor trust funds; hospitals; and other health care services needed by employees and their dependents and by the public at large. The New York Business Group on Health was one of the first coalitions to emphasize that the malpractice problem impinges on each of these areas of concern, and addresses the problem through workshops, conferences, and publications. The coalition has worked closely with a number of other organizations in the metropolitan area and has shared information with others around the country. From this perspective, the malpractice problem comprises two sets of intertwined but essentially different issues. The first includes the financial impact—insurance, litigation, and the effects on the availability and quality of care—and is addressed by tort reform. The second issue, to which much less attention has been paid, is part of the broader problem of the quality of care. It includes the definition of standards of practice and quality assurance and is addressed by eliminating malpractice by appropriate preventive measures such as removing the licenses of practitioners and institutions that fail to abide by those standards.

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The first set of issues are quite familiar. Costs of health care are increased by the passage of the escalating malpractice insurance premiums and the much larger costs of defensive medicine to both patients and payers. As the pressure to contain costs rises, and facing the necessity of allocating health services, it is unconscionable to waste health care dollars on items that do not contribute to health. The increasing costs and inequities of the present tort system result in approximately 28% of the award dollar reaching the victim of the declared malpractice, with the remainder going to legal costs and insurance expense. Many victims of malpractice actually receive nothing. There is validity in its designation as a lottery both for those who win the multimillion dollar awards and for the lawyers who press these claims. One should also not forget the intangible costs of litigation to the victims who must wait years for the adjudication of their claims and to the physicians and others who sacrifice precious time and energy and sometimes their reputations as well in defending claims that are not really valid.

Malpractice insurance raises such issues as validating the need for high premiums. When a claim is made, coverage is actually less costly in the long run than coverage of occurrences. What happens when reserves are inadequate and carriers are threatened by bankruptcy? The availability of health services then becomes an issue. For example, according to the American College of Obstetricians and Gynecologists, 23% of obstetricians around the country have stopped providing obstetrical care. Other specialists are turning away high risk cases. Young physicians are said to avoid establishing practices in high cost areas like New York State, and older physicians are reputed to be retiring rather than maintain the level of activity required to cover their malpractice insurance premiums.

Quality also becomes an issue when patients must be exposed to the potential of unnecessary diagnostic and therapeutic manipulations. Of course, there are those who argue that the threat of malpractice is probably the strongest factor in maintaining quality. However, that may not necessarily be the consensus. Industry is beginning to recognize these issues and to explore various suggestions for tort reform that have been proposed. The Medicine Business Coalition of New York State, in which businesses and the Medical Society of the State of New York have joined, has studied these problems. The Business Council of New York State is another group that has studied these problems and has produced a statement that supports the kinds of tort reform that would reduce both the cost of litigation

and the amount of the awards. Support for such reform has grown particularly in the past year or two as similar problems have arisen with product liability, environmental liability, and municipal liability. These are areas in which the employer is much more directly involved as the payer.

The erosion of quality of care must be addressed by first defining standards of practice and the prevention of malpractice. If not addressed by health professionals, solutions to the problems will be imposed on them by lay administrators, bureaucrats, and regulators who may lack expertise in the art and science of medical practice. How does one develop standards of care? The classic examples of bad care are easily recognized after the fact: the operation on the wrong patient or the wrong leg; the patient with brain damage because the wrong anesthetic was given; an instrument left in the body; failure to make an obvious diagnosis; delay in appropriate treatment because the seriousness of the medical problem was not recognized. But are outcomes always a reliable criteria? Those cases in which patients survived truly atrocious treatment are well known, as are those in which patients failed to survive the best treatment. Standards of care encompass the competence of the physician. However, that competence may be eroded by age or disuse, or the physician may be one of the estimated 15% of practitioners alleged to be victims of alcohol or drug abuse. Is bad care the application of an outmoded treatment proven to be ineffective or the use of a new inadequately tested treatment, or is it outright quackery? Industry is learning a great deal about the pattern of practice from second surgical opinion programs and utilization review programs. Given the broad variations depicted by small area analyses of utilization, it may be difficult to determine appropriate treatment; however, it is obvious that both extremes cannot be correct.

Is the incidence of malpractice increasing? Or does the increase in claims merely represent the litigiousness of society augmented by the case finding of plaintiffs' attorneys? Although the answer is not really known, the increase may be attributable to the unreasonable expectations of patients and their families resulting from media depictions of the "wonders of medical science." To some extent it probably reflects the breakdown in patient-physician relationships due to overspecialization and depersonalization and fragmentation of care. In part it may also be indicative of the improved documentation now required by third party payers and the peer review process which is facilitated by improvements in medical record systems.

What may be the most important effort to reduce the incidence of malpractice is the development of profiles for individual practitioners and institutions that allow analysts to identify undesirable patterns of practice. Industry is beginning to develop judgments from such analyses not as a basis for initiating malpractice claims but to steer employees and their dependents toward the more effective physicians and hospitals, or at least away from those branded as less than optimal, and to determine the type of treatment they are to receive.

The American public continues to have a high regard for the quality of its health care system. Physicians and other health professionals will have to work harder and faster to develop acceptable standards of practice and become much more militant in identifying those who repeatedly fail to meet those standards if they wish to retain this high level of regard. They will also have to be much more aggressive in strengthening the professional disciplinary measures that will get those who repeatedly fail these standards out of the system. Unfortunately, accidents will continue to occur, and their victims should be promptly and appropriately compensated. Tort reforms are needed to reduce the number and costs of claims but in the last analysis the real solution is the assurance of quality care. To continue to win the support of industry for tort reforms they are proposing, health professionals and their organizations must devote their attention to the development of appropriate standards of practice and a much more aggressive effort to see that they are followed.

Current issues in medical malpractice confronting hospital administrators

HAROLD L. LIGHT

Before the famous "Darling" decision in 1965, hospital administrators did not have to concern themselves with medical malpractice or, for that matter, any malpractice committed within their institutions.[1] From the time of that decision until the issuance of sections 2805J and 2805K of the New York State Public Health Law, there has been a steady increase in the degree of responsibility imposed on hospitals in the area of medical malpractice. The hospital administrator is viewed as essential in carrying out the mission of government that has, in this manner, tacitly acknowledged its own inability to adequately monitor the performance of medical professionals.

Hospital management has been described by Drucker and Bays as the most difficult managerial job extant,[2] most likely because, contrary to what exists in a normal managerial situation, the hospital manager does not control the principal means of production. It is no secret that hospitals depend on inpatient activity for their income. It is also no secret that even in this time of enlightened consumerism it is the practicing physician who determines the need for hospitalization and who, more often than not, determines the institution at which that hospitalization takes place. Thus, even in New York City where many teaching hospitals have large cadres of full-time physicians, it is the unsalaried, voluntary attending staff whose admissions produce the bulk of the hospital's income. These individualists, almost all of whom have many hospital appointments, have always been relatively free to admit patients to the hospital of their choice. In today's climate, at least for the short term and before further inevitable bed decertifications and hospital closings take place, the practitioner will have an even greater ability to admit patients to the institution of his or her choice.

How then is the hospital administrator to deal with the requirements imposed by government? How is the administrator to deal with the requirements of his or her own governing authority to conform to the law? How is the administrator to protect the institution from economic disaster in the form of disclosures that will inevitably lead to malpractice or other liability actions with attendant publicity as the latest factor with which to contend? At the same time the administrator must try to improve relationships with the medical staff, by developing joint ventures with the staff and giving them the ever increasing voice they often seek in the development of hospital policy.

The hospital administrator cannot satisfy all of the parties identified above and survive. I believe that fact is reflected in the escalating rate of involuntary turnover of chief executive officers that is evident throughout New York State, as well as the rest of the country. It may be true, as some suggest, that many of the surviving chief executive officers' problems will disappear when the predicted glut of physicians becomes a reality, and when the hospital system has shrunk to its irreducible minimum. However, the intervening years before those events take place can only be cause for great concern to the operating executives and to the governing authorities of hospitals.

As if things were not bad enough, the climate for liability insurance for institutions and their directors and officers is such that there is significantly less commercial insurance available now than in the past. That coverage is available at rates that are in excess of 300% over previous years. The most recent legislation enacted by the New York State Legislature makes the hospital the excess insurer for all of the physicians on the staff who choose to have such coverage. It imposes yet another economic responsibility on the hospital with less than total reimbursement being made to the hospital and with a declining capability of purchasing excess coverage for the increased exposure.

What the State of New York has effectively done in its formulation of a solution to the medical malpractice crisis, is to announce to the world and to codify in law the notion that hospitals, irrespective of the fact that they may have had no responsibility for liability in a given malpractice situation, will be the "deep pocket" in which plaintiffs and their attorneys may fish for punitive or other damages, real or imagined, which may be awarded on the basis of whim or emotion by juries or judges. The State of New York has also said through this law that a single group of individuals, the practicing physicians of a community, should be afforded protection from personal liability by the taxpayer irrespective of their level of competence or the degree of their personal responsibility in a particular malpractice action. It does so, in this instance, through the hospital reimbursement methodology as opposed to general tax levy monies. Why the medical community should be singled out for this type of protection while others are not is an important philosophical question that needs to be

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discussed. Suffice it to say that the man or woman on the street when asked if they would like their tax dollars used to protect one of the highest income earning professions, would most likely indicate personal antagonism for the projected solution. It is no wonder that cynics in the health care industry believe the political solution that has been promulgated was done to disguise the funding mechanism and to offset some of the costs to New York State by capturing Medicare and Medicaid funds.

From an operational standpoint, the role of the hospital administrator, which is difficult at best to begin with, is becoming both more difficult and more hazardous. If the administrator abides by the law and reports all incidents as required by the New York State Hospital Code, it is done so with full knowledge that such information is no longer protected by the Freedom of Information laws and is, therefore, discoverable by plaintiffs' attorneys. Obeying the law exposes the administrator, the institution, and its trustees to potential liabilities that did not heretofore exist. The potential economic harm to the institution is self evident in such a scenario as is the potential harm stemming from the negative public relations image that may be created by a stated policy of New York State that exposes hospital deficiencies to the mass media.

The imposition of responsibility on the hospital administrator to report "impaired physicians" is, similarly, a condition that can only exacerbate existing tensions between the administrator and the medical staff. If the administrator fails to report a physician who is subsequently found to be impaired, he once again subjects his institution, himself, and the governing authority to potential liability. On the other hand, the reporting of physicians suspected of being impaired may lead to law suits and the attendant economic risks that implies and, perhaps as important as all of the above, a hostile reaction from other members of the medical staff who see themselves as potentially exposed in the future.

From the physician's standpoint, the shift in the balance of power that he may see as resulting from an impending "physician glut" projects out to a decline in income, an increasing lack of control over his own destiny, his own fees, increased regulation by government and hospitals, and the skyrocketing costs of malpractice insurance premiums. All of the above lead to less professional satisfaction and a high level of anxiety. The logical target on whom to vent all anxieties and frustrations is the hospital administrator who is, after all, close at hand, is the one who generates the actions required by the state and the governing authority and, generally, is the most vulnerable of the forces involved in this interplay.

Last, but hardly far from least, is the inability of the hospital administrator to recapture sudden and unanticipated operational costs over which the administrator has no control. The escalating costs of both malpractice insurance for the hospital and all general liability insurance are costs that the hospital cannot recapture in the prospective payment methodology now in place for Medicare and soon to be in place for Medicaid and Blue Cross as well. The increased costs attributable directly to premium escalation as well as the indirect cost of interest resulting from borrowings necessary to pay excess insurance premium costs for physicians on the staff of hospitals requesting it, all must be found within the hospital's existing budget. This often results in taking money away from other existing programs within the hospital.

For the administrator, then, this is a no-win situation. He is faced with increased responsibilities, increased costs in the operation of his hospital, increased surveillance of his performance by regulating authorities with resultant personal as well as professional liability, and increased antagonism from those on whom he is most dependent for successful performance. It is not surprising that the administrator of the future is most likely to come from the ranks of industry and its "bottom line mentality" rather than from the hospital field itself. Those who entered the field out of a desire to see that a societal need was met and that high quality health care was the product being delivered cannot help but be discouraged and disillusioned by the trends that confront us today.

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Hospitals under the regulatory knife: Directions in medical malpractice

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In response to the crisis in medical malpractice, there has been a major policy shift toward increasing hospital accountability for the actions of physicians in New York State. This shift is evident in recent State laws and regulatory requirements that delineate hospital responsibility for the quality of care provided by physicians and the purchase of excess malpractice insurance coverage for physicians. Although the role of the hospital in malpractice prevention is critical, such legal and regulatory directions ignore the fundamental reasons for the medical malpractice crisis. And by doing so, the solutions to the problem are not being addressed. Additionally, there has been no relief for the hospitals as they face their own malpractice insurance crisis. The intent of this paper is to highlight the reasons for the malpractice crisis, describe the responsibilities of the hospital for physician malpractice control, and address the problems yet to be resolved by the State's recent attempts at malpractice reform.

THE MALPRACTICE PROBLEM

The rapid growth in the frequency of claims, the size of malpractice awards, and the number of unfounded suits indicates a problem with the current malpractice system. The burden of the rising costs of malpractice is clearly being passed on to the already costly health care system and the citizens of New York State. Unfortunately, of the millions of dollars that are spent each year on medical malpractice, it is estimated that only a small portion, somewhere around 20%, is retained by the injured person.[1] These costs, which result in increased premiums or funding requirements for self-insurance, are ultimately borne by the consumer because they are built into the cost of the hospital stay or the physician visit.

Malpractice insurance rates have been increasing nationwide and particularly in New York State. Insurance experts indicate that, generally, rates are rising about 25 to 30% per year.[2] New York has experienced greater medical malpractice insurance losses than other states. In 1983, New York insurers paid out $157.10 in claims for every $100 of malpractice premiums received, compared with a national average of $106.10.[2] That is a difference of 48%. Behind these rising rates is the fact that both the frequency and severity (cost per claim) of claims have been growing steadily.

The St Paul (MN) Fire and Marine Insurance Co, the nation's largest medical malpractice insurer, reported that the average cost of incurred claims against its 1,550 insured hospitals nearly doubled from $6,892 to $12,785 between 1979 and 1983.[3] Jury Verdict Research of Solon, OH reported that the mean malpractice settlement was $367,319 in 1979 and $962,258 in 1982. In 1979, there were 134 verdicts in the plaintiffs' favor, 14 of which involved settlements greater than $1 million. In 1982, there were 234 verdicts in the plaintiffs' favor with 45 resulting in settlements greater than $1 million.[4] To some degree, the size of the awards rises with the cost of providing health care.

The impact of the growing dollar amount of claims is aggravated by the rise in the frequency of claims filed against hospitals. Hospitals insured by the St Paul Company incurred three claims per 100 hospital beds in 1983, as compared with 1.6 claims per 100 beds in 1979.[3] For New York State in 1984, there was a frequency of five to six claims per 100 beds and for New York City (including Nassau County), the frequency dramatically increased to between ten and 12 claims per 100 beds.

Over the past seven to eight years, actuarial estimates indicate that the claims frequency in New York City has increased about 3 to 4% per year and claim severity between 20 to 22% per year, resulting in a compounded increase of about 25% per year in malpractice dollars for losses. In New York State, the average claim cost arising during calendar year 1984 is estimated to be $120,000. Actuarial predictions for average costs of claims filed this year and settled in the future in New York City are estimated to be $400,000. In terms of total malpractice insurance dollars, actuarial averages for 1984 reveal costs of between $5,000 and $10,000 per hospital bed in New York City.*

The combination of the increasing number of claims and their rising cost is resulting in dramatic changes in the availability and affordability of malpractice insurance coverage. These changes include a reduction in the number of insurers available for New York hospitals, exorbitant price increases in primary and excess insurance, and the movement to writing insurance on a "claims made" basis.

The number of malpractice insurers willing or able to do business in New York is rapidly shrinking. Due to the high cost of losses and loss expenses, and the inability to

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* Estimates provided by James Stergiou, President, Woodward and Fondiller, actuarial consultants; Fellow of the Casualty Actuarial Society; and Member of the Association Academy of Actuaries.

cover these costs through the investment of premium funds, insurers have been facing insolvency and pulling out of the market. The problem has resulted in a large part from the insurers' inability to accurately estimate their potential malpractice claim losses.[4] Since most malpractice insurance was written on an "occurrence" basis, the claims filed many years after the covered period were significantly underestimated. In these policies, the insurer covers the insured for all claims that arise out of the acts or omissions that occur during the policy period, even though the claims arise subsequent to the period.

Many New York hospitals are now experiencing financial and legal problems arising from the insolvency of two malpractice carriers, the Ambassador Insurance Company and its wholly-owned subsidiary, Horizon Insurance Company.[5] These hospitals are now either self-insured or uninsured for claims that were previously insured. Due to the prohibitive expense of retroactive insurance, this will not be a feasible means of protection against insolvent carriers. The hospitals have little alternative but to use their own assets to satisfy and defend malpractice claims. Most hospital financings require the maintenance of insurance or an acceptable program of self-insurance. The absence of insurance or a fund of self-insurance may interfere with the ability to obtain short- and long-term loans.

The history on the physician malpractice insurance side has been similar and foretelling. Employers Insurance of Wausau, WI, which had underwritten the New York State Medical Society's Malpractice Insurance Program for 25 years, decided to discontinue business in New York in 1973. Argonaut Insurance Company agreed to provide coverage, but at rates 93.5% higher than previously available.[6] An additional increase of 200% was requested in 1974, and soon after, Argonaut also abandoned the market in New York.

The premium costs for excess insurance to cover liability for amounts greater than that provided by the primary or self-insurance have skyrocketed. Excess rates have doubled in New York City, according to several insurance brokers servicing New York (personal observation). At one 200-bed hospital, the excess premium jumped from $40,000 to $80,000 between 1983 and 1984. This premium cost the hospital $150,000 for 1985. According to Joseph J. Baumann, Inc, insurance brokers and consultants, at one 500-bed hospital, the excess rates rose from $85,000 to $190,000 between 1983 and 1984. Coupled with these rate increases has been the reduction in available coverage. About a dozen major insurers are no longer writing excess malpractice insurance in New York. Hospitals are struggling to find coverage and therefore must self-insure for a higher level of losses.

As a result of trends in insurers' loss experience, insurers are moving to write insurance on a "claims made" basis. This underwriting method only covers malpractice claims actually filed during the insurance period. Claims made later will be covered in subsequent periods when premium prices will reflect the inflated cost of the claims. It will, however, continue to be difficult to estimate potential losses because claims can take many years to reach settlement. Most of the hospitals' excess coverage will be renewed on a "claims-made" rather than "occurrence" basis. A disadvantage of a policy based on claims-made coverage for hospitals is that at the end of the policy period, the hospital is without insurance protection for those claims that are not asserted until a time subsequent to the policy period. To cover such situations, the hospital must purchase "tail coverage," which is usually expensive due to the uncertainty of the cost of future claims.

Lack of Financial Relief for Hospitals

Between 1983 and 1985, hospitals in New York were reimbursed for inpatient services by Medicare, Medicaid, and Blue Cross according to the New York Prospective Hospital Reimbursement Methodology (NYPHRM). The reimbursement for hospital malpractice insurance produced by this system is grossly inadequate to cover rising costs. The level of reimbursement under NYPHRM is set on the basis of 1981 costs inflated annually by a trend factor. The trend factor is comprised of two components that recognize a portion of the increase in malpractice insurance costs. These components include the average weight of malpractice insurance cost as a percentage of total operating costs for specific groups of hospitals, and a price movement index derived from a New York State Department of Health Office of Health Systems Management (OHSM) survey.

There are indications that the rate of increase in malpractice insurance premiums and reserve fund requirements for the self-insured has significantly outpaced any increase in reimbursement provided by the trend factor. Due to the reimbursement constraints under NYPHRM imposed by the fixed 1981 base-year costs, hospitals are not being adequately reimbursed for the increases in malpractice costs from the major third party payers. This means that hospitals are not able to pay the costs of malpractice insurance without potentially significant reductions in other hospital operating expenses. Hospitals may be forced to be underinsured or uninsured if cost reductions in other areas (including patient care) or new revenue sources cannot be achieved. In 1986, NYPHRM continues for the non-Medicare payers while the Federal Medicare Prospective Payment System (PPS) determines Medicare reimbursement.

It is not likely under the current reimbursement system that the situation will improve in 1986 or beyond. New York hospitals will probably see only small increases in the reimbursement rates over the next few years due to lower rates of inflation and more stringent third party regulations. Secondly, there will be a significant time lag, approximately five to seven years, before the benefits of malpractice tort law changes will appear in hospital expenditures. Unless there is a change in the reimbursement methodology to recognize the already occurring and anticipated sharp increases in malpractice costs, the burden of these additional costs will continue to fall unfairly on hospitals.

Compounding the problem of inadequate reimbursement for hospital malpractice costs is the enactment of Section 19 of the Malpractice Reform Act of July 1, 1985. This legislation required that hospitals purchase excess malpractice coverage for physicians primarily affiliated with them who request such coverage and have the requisite level of primary coverage. Section 19 was offered in

response to widespread discontent by physicians in New York State, particularly those upstate, about rising malpractice premiums and the inability to obtain adequate coverage. Physicians such as neurosurgeons, obstetricians, and orthopedic surgeons threatened to leave their practices, cease doing surgery, or reject patients due to the huge increase in liability premiums. Although this problem involved the increased cost of primary levels of coverage, Section 19 only addressed the adequacy of coverage through guaranteeing provision of excess coverage. It was only intended as a temporary measure.

The legislation does provide an adjustment to the hospital inpatient rates to reimburse the hospitals for these costs. However, the construction of the law has not guaranteed payment in full to the hospitals. The Federal government has denied Medicare participation in assuming a share of these costs. The hospitals were directed by the State to increase charges to the charge payers in order to cover their share of these costs. However, the hospitals were limited in their ability to raise charges to the extent necessary to cover the share attributable to these patients. Although the premium was retroactive to July 1, 1985, the number of interested physicians and related costs could not be resolved until the end of 1985. Therefore, a significant burden of these costs falls on the hospitals. In addition, there has been a delay by the third party payers in issuing the required rate adjustments. This has had a major impact on hospital cash flow.

Section 19 has not been the centerpiece of the critically needed malpractice reforms in New York State. In many cases, it provided physicians with something they did not even seek. This provision has never been a major consideration in physicians' decisions to continue to practice medicine in New York. The hospital industry is opposed to any extension of Section 19 and has offered legislative alternatives for funding and providing excess medical liability coverage for physicians.

Hospital Accountability for Physician Malpractice

In New York State, hospital responsibility for physician malpractice is set forth in Public Health, Education, and Malpractice legislation. Hospitals have always been actively involved in monitoring the quality of care provided to their patients by all of their staff including attending physicians, residents, and nurses. However, recent changes in the law and regulatory requirements have increased hospital accountability for physician malpractice. The following are examples of such changes.

The Malpractice Reform Act of 1985. This provided for several major changes to the Public Health and Education Laws. These basic provisions governing hospital responsibilities for malpractice prevention, monitoring, and reporting include the following:

- Section 2803-e requires hospitals and other facilities to report incidents of possible professional misconduct by physicians and medical residents within 30 days. Medical residents were added to the existing language in 1985.
- Section 2805-j requires hospitals to develop a coordinated program to identify and prevent medical and dental malpractice. The State requires that medical and dental malpractice prevention programs provide for the establishment of a quality assurance committee responsible for reviewing services rendered in the hospital and coordinating malpractice prevention programs; the development of a medical and staff privileges sanction procedure through which credentials, physical and mental capacity, and competence in delivering health care services are periodically reviewed as part of an evaluation of staff privileges; the maintenance and continuous collection of information concerning the hospital's experience with negative health outcomes and incidents injurious to patients; and the provision of education programs regarding malpractice and prevention.
- Section 2805-k requires hospitals to complete investigations of practitioners prior to granting or renewing professional privileges. Information regarding a physician's previous employment, pending misconduct proceedings, and pending malpractice actions must be provided by the physician and reviewed by the hospital. Hospitals must provide information, as defined in this section, when requested by another institution.
- Section 19 requires hospitals to purchase excess malpractice insurance coverage for all physicians primarily affiliated with the hospital who request such coverage. Although this provision calls for adjusted payment rates to cover this purchase, hospitals have experienced severe cash flow problems due to delays in payment. Additionally, the recovery of full reimbursement to cover these costs is improbable due to the denial of financial participation by Medicare and the method of cost allocation to the other payers. Hospitals across New York State are seeking repeal of this provision.

The incident reporting regulation. Implemented in 1985, it requires hospitals to report emergencies and other incidents that threaten the safety of patients or staff in the hospitals within 24 hours by telephone to the New York State Department of Health. Incidents that must be reported include patient deaths or impairments of bodily function in circumstances not related to the natural course of illness, disease, or proper treatment; equipment malfunction during treatment or diagnosis of a patient that did or could have adversely affected a patient or health facility personnel; poisoning occurring within the facility; and strikes by facility staff.

Written notification must be sent to the Department of Health within five days of the initial telephone contact and the hospital must both conduct an internal investigation and forward the results to the New York State Department of Health. Information provided as part of this reporting system permits the Department of Health to monitor incident patterns in hospitals and, in particular, with certain physicians. While hospitals have significant reservations about this new regulation, they are prepared to fully participate in the 18-month demonstration.

New regulations governing graduate medical education. Adopted in 1985, these regulations allow hospitals to permit residents and medical students to perform a service for which a license is required only if they are under the direct control and supervision of a licensed physician.

Hospitals must also monitor physicians based on criteria set forth by Title 8: the Education Law on professional misconduct, including the following: obtaining a license fraudulently; practicing the profession fraudulently beyond its authorized scope, with gross incompetence, with gross negligence on a particular occasion, or negligence or incompetence on more than one occasion; practicing the profession while impaired by alcohol, drugs, physical disability, or mental disability; being habitually drunk or being an abuser of drugs; and if a physician has been found

guilty of improper professional practice or misconduct or has had his or her license to practice medicine revoked, suspended, or any other disciplinary action taken in another state.

Hospitals are required to report all incidents of professional misconduct to the appropriate State agency.

The Joint Commission on Accreditation of Hospitals (JCAH) sets forth medical staff credentialling requirements. The medical staff bylaws must contain criteria for granting initial or continuing staff membership. Such criteria must include evidence of current licensure, relevant training and experience, current competence, and health status. The JCAH recommends that information provided by all applicants, regardless of whether they seek an initial or continuing appointment, include: 1) involvement in any professional liability action; 2) previously successful or currently pending charges to any licensure or registration; and 3) loss of medical staff membership or clinical privileges at another institution. The process for delineation of privileges must be clearly defined in the medical staff bylaws.

The JCAH also requires that the medical staff complete a wide range of quality assurance activities to monitor and evaluate the quality and appropriateness of patient care and the clinical performance of all individuals with clinical privileges. Monthly departmental meetings must be held. In addition, surgical case reviews, blood usage reviews, and antibiotic usage reviews must also be performed.

In addition to the many requirements for medical staff, the JCAH also mandates that all areas of the hospital perform quality assurance activities. The requirements for departmental compliance are clearly defined in the JCAH manual. Specific hospital-wide functions include such activities as infection control programs, utilization review, and review of accidents, injuries, and safety hazards. Additionally, the quality of the clinical performance of those individuals who are not permitted by the hospital to practice independently is monitored and evaluated as part of the overall quality assurance program.

An additional set of standards and requirements that hospitals with teaching programs must meet are those established by the Liaison Committee for Graduate Medical Education (LCGME). This agency accredits each residency program through its Residency Review Committee (RRC) structure. Minimum standards for supervision of residents and the amount of ongoing academic instruction are established by each discipline. On-site reviews are held and programs may be accredited for up to three years.

In addition to State laws, the JCAH, and the LCGME, there are several other outside agencies that monitor the quality of care delivered in hospitals, including the Peer Review Organization and the Medicaid Utilization Review agents.

The Peer Review Organization (PRO), established by Federal statute in 1982, is charged with monitoring the utilization and quality of care delivered to Medicare beneficiaries in hospitals nationwide. In New York State, the PRO became operational in September of 1984 and since then has been reviewing almost 40% of Medicare cases statewide. As part of its review plan, the PRO contracted to meet discrete quality of care review objectives, as well as to review all cases for "generic" quality concerns. The PRO, through its review processes and data consistent with Federal regulations, can "sanction" a practitioner providing sufficient evidence of delivery of poor quality care exists. The provider or practitioner is therefore excluded from receiving payments from the Medicare program because of a significant lapse in the quality of care delivered to Medicare beneficiaries.

Additionally, the New York State Department of Health contracts with several utilization review agents to perform review of utilization of Medicaid benefits. Included in the review plans for these agents are objectives with which the quality of care rendered is adjudged simultaneously with the review for utilization of benefits.

It is clearly in the interest of every hospital to assure that the highest quality of patient care is provided. A hospital shares liability in most malpractice cases brought against any of its physicians for services rendered in the hospital and, therefore, may be at great financial risk. The following hospital policies and procedures serve this effort to ensure quality care.

Internal hospital quality assurance programs. In order to comply with all applicable laws and regulations, JCAH standards, and residency program requirements, hospitals have developed sophisticated quality assurance and risk management programs. Each governing body has established a committee responsible for monitoring and evaluating the quality of care delivered in the institution. Separate departments of quality assurance and risk management have been established. Quality assurance committees usually function at several levels, and in order to meet the multiplicity of requirements, have established subcommittees responsible for specific functions.

Compliance with outside agencies. A hospital's compliance with state laws and JCAH and residency program requirements is closely monitored. The JCAH surveys each hospital at least every three years. The New York State Department of Health inspects each hospital at least every three years and usually much more frequently. Residencies may be accredited for a maximum of three years. In order for hospitals to receive accreditation and reimbursement, favorable survey outcomes are essential.

Hospital credentialling policies. In an attempt to improve the quality of care rendered at facilities, hospitals constantly upgrade their initial and continuing credentialling processes. These include meeting JCAH standards and state law regarding review of all pending malpractice actions, as well as conducting peer review and monitoring patient outcomes. Hospitals are now linking a practitioner's performance under quality assurance and utilization review to this important process.

Hospital procedures on supervision of resident staff. Hospitals with teaching programs provide licensed attending physicians as supervisors of the care ordered and delivered by residents. Ordinarily, for patients without personal physicians, a senior and one or more junior residents and several medical students comprise the team that is supervised by an attending physician. These attendings are required to visit the patients under their team's care and discuss desirable courses of treatment and write admission notes, and at least weekly progress notes. They are charged with the direct supervision of the care rendered

by their team. In some institutions, in addition to the resident team, a private physician is assigned to a patient who does not have one.

For patients with personal physicians on staff at the hospital, there are teams as well, with the personal physician serving as the supervising attending. Residents in training and under this supervision are permitted to order tests, medications, examinations, surgery, other invasive interventions, and to give injections and provide all other aspects of care appropriate to their profession. They are the focal point of 24-hour care at teaching hospitals. In hospitals without teaching programs (nonteaching hospitals), care is given directly by the patient's private physician and coverage is provided by salaried, licensed physicians.

Problems Requiring Resolution

New York State is placing increased emphasis on hospital accountability for the actions of the medical profession in order to ameliorate the malpractice crisis. This may help somewhat, but it is not the only solution needed. Some experts indicate that improved state procedures for medical discipline and licensing are essential for cracking down on physician incompetency and negligent patient care. However, there is currently an abundance of laws, regulations, and oversight activities addressing the quality control of medical practice. Attention now needs to focus on meaningful reform to the malpractice system.

In order to curtail the dramatic growth in malpractice costs, it is necessary to make insurance less costly and the legal system more just, through malpractice reform. The following areas of malpractice reform are considered to be the most effective methods of reducing the size and frequency of malpractice claims.

A cap on pain and suffering. Placing a limit on the amount of awards for noneconomic damages or pain and suffering may be one of the most effective tort reforms in reducing the size of awards. Noneconomic damages represent the intangible losses over and above medical costs and lost income. Awards for pain and suffering raise verdicts and attorneys' fees to exorbitant levels. It is estimated that there may be a savings of 30 to 35% of loss costs with a cap of $100,000 on awards for pain and suffering. With a cap of $200,000, the savings remain significant at an estimated 20 to 25% of loss costs.* The cap on noneconomic damages in California ($250,000) was upheld as constitutional by the State Supreme Court as a legitimate way to curb medical costs.

Elimination of joint and several liability. New York State law presently allows a plaintiff to seek payment in total from any one or all of the joint tortfeasor defendants. This is the doctrine of joint and several liability. Therefore, even though a hospital may be found to be only tangentially involved in an action, there is exposure to a much larger liability if a codefendant is not solvent. Hospitals are frequently seen as the "deep pocket" when the physician codefendants have exhausted the limits of their policies or have reached an individual settlement during the litigation process. Some states have abolished the joint and several rule by statute. Other states have substituted a rule of several liability that allocates damages in proportion to each defendant's fault.

Limitation on attorney fees. The contingency fee is the most common arrangement for payment of plaintiff attorney fees in malpractice cases. This fee is the agreed-on percentage (usually about one third) of any final award or settlement for the plaintiff. The Malpractice Reform Act, passed in 1985, included a provision to limit the attorney's share as the award increases. However, this was only a modest reduction and represented a watered-down version of original proposals. Further limitations in this area are needed.

Also yet to be resolved is the question of who will pay for the significant rise in hospital malpractice costs not covered by the present reimbursement system and the purchase of excess coverage for physicians mandated by Section 19 of the Malpractice Reform Act. The burden of these costs now falls on the hospitals and, if not adequately recognized by the third party payers, the hospital industry in New York State could be facing financial instability.

The hospitals in New York are directed by a multitude of laws and regulations to ensure the quality of patient care and provide oversight of physician activities. There are sufficient state controls in this area and, therefore, efforts must be directed to malpractice reform. Meaningful malpractice reform is critical in New York State in order to curtail the runaway costs of malpractice and ensure a just legal system.

* Estimates provided by James Stergiou, President, Woodward and Fondiller, actuarial consultants; Fellow of the Casualty Actuarial Society; and Member of the Association Academy of Actuaries.

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The history of medical malpractice in New York State

A perspective from the publications of the Medical Society of the State of New York

SANDRA CIRINCIONE

It is often said that if two or more physicians gather, they will inevitably discuss the malpractice crisis; this is probably true. The state of the malpractice crisis affects the way physicians practice, their relationships with patients, the cost of services, and even the type of services they will render. As other interest groups, such as lawyers and consumer groups, strive to make their opinions heard, and legislators around the country attempt to grapple with this persistent problem, physicians have been forced to include malpractice as a daily factor of their lives.

Others may wonder why the malpractice crisis grew to such proportions in such a short time. Physicians who know better point out that the current crisis did not suddenly materialize but has been an issue of concern to the medical community since malpractice insurers began leaving the industry in the early 1970s. However, even many physicians may not realize that organized medicine's concern about medical malpractice has a history almost as old as the Medical Society of the State of New York itself.

The *New York State Journal of Medicine* was first published by the New York State Medical Association in 1901. A brief historical summary is necessary to explain the relationship between this organization and the Society. The Medical Society of the State of New York was formed as a result of an act of the state legislature in 1806.[1] The Society's business, meetings, and scientific reports were published in The *Transactions of the Medical Society of the State of New York*, a publication that was produced annually from 1807 to 1905.

In 1884, a dispute arose between the Society and the American Medical Association, resulting in the severance of ties between the two bodies. This event led to an upheaval in the Society, for some members did not approve of the Society's decision to break with the organization that had been formed specifically to unify the medical profession across the nation. These members split from the Society in 1884 and formed the New York State Medical Association, which maintained relations with the AMA. In 1901, the New York State Medical Association began publishing a record of its transactions in the *New York State Journal of Medicine*.[2]

The Society and the Association remained separate entities until 1905. In 1903 the two organizations, expressing a desire to reunite, formed a joint committee to develop a plan for consolidation. After state legislation was passed allowing the two organizations to merge, a proposal developed by the joint committee was submitted for a referendum vote to both organizations. The vote passed both organizations by wide majorities, and in 1905 they were unified into the Medical Society of the State of New York. The new organization retained the Society's original seal, but adopted the *New York State Journal of Medicine* as its official publication.[3]

In going through the volumes of both the *Transactions of the Medical Society of the State of New York*, the Society's original publication, and the *Journal*, one discovers that malpractice has been addressed since almost the beginning of the Society. Many of the early references deal with quackery, but some of the issues discussed are startlingly similar to the malpractice problems of today. The present day malpractice problem has come about with the evolution of medical education and technology. By studying the texts, one can trace the evolution of malpractice from early in the Society's history to its current proportions. This history also gives glimpses of the origins of peer review, monitoring of scientific progress, and a view of medicine as it evolved into the science it is today.

HISTORY OF MALPRACTICE IN THE *TRANSACTIONS OF THE MEDICAL SOCIETY OF THE STATE OF NEW YORK*

From 1807 to 1850. Since its early days, the Society has been involved with the issue of malpractice. The first journal article that refers to malpractice appeared in the *Transactions* of 1822, in a report from the committee of academies, colleges, and common schools, in a reference to the powers of county medical societies.[4] By legislation enacted in 1818, censors from the districts of the State Society (representatives of the county societies) were responsible for reviewing medical students who wished to be licensed as physicians. On approval of the censors, the students were referred to the State Society as candidates for licensure. Physicians were required by the state to be associated with the local society in the county in which they lived, "in order, no doubt, that they may be subject to the wholesome discipline, which said societies are authorized to enforce," the report read, "but it is equally certain, that said act contains no penal provisions for non-compliance with its requisitions . . . They [the authors of the report] moreover respectfully suggest, that the honorable Legislature be informed that although the several incorporated Medical Societies possess the power by law to grant licenses to practice physic and surgery, they possess no effective control over the members of the profession, and cannot therefore prevent abuses which may be practiced by them; they therefore recommend that the law be amended, that the several County Medical Societies be empowered by law to suspend from the exercise of the pro-

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fession, any persons notoriously known to be guilty of dishonest conduct, habitual malpractice, or habitual intoxification, or charged with infamous offenses, in order that the profession may be purged of its unworthy and incompetent members."[4]

It seems clear the authors of the above report were referring to malpractice and not quackery when an 1830 report dealing with this right is examined.[5] The report concerns an upstate physician who was criminally indicted and also expelled by the county medical society for gross misconduct involving a possibly induced abortion and a criminal and adulterous affair with the wife of another man. The physician protested the expulsion, saying the proceedings by the Society were unconstitutional and inappropriate because he was acquitted of the legal charges against him. The court of common pleas of the involved county reviewing the proceedings and decision against the physician of the county medical society, ruled that, "The law providing for the expulsion of physicians from medical societies, and the abrogation of their licenses in cases of gross ignorance or misconduct in their profession, or when guilty of immoral conduct or habits, is a valid and constitutional law. . . . A medical society is not precluded from preferring charges against a physician, by the fact of the same charges having been once before passed upon by them, and not sustained. The trial and acquittal of a physician in a court of criminal jurisdiction, upon the same charges exhibited against him by a medical society, are no bar to an inquiry under the statute for the purpose of depriving him of his right to practice physic and surgery."[5]

From 1851 to 1899. In 1872, the first direct and extended commentary on malpractice was delivered by the Society president, William C. Wey, MD, in his anniversary address to the 66th annual meeting of the Society.[6] Physicians, as all other members of the business community, have certain responsibilities and liabilities involved in the work the community contracts with them to perform. Moreover, Wey stated, as a more educated, more influential member of the community, the physician's "obligations are increased with the varied and expanded character of his interests in the community." Physicians do not object to the fair regulation of their services, but "we have reason . . . to complain of a harsh and unjustifiable construction of its spirit and intention, as if, in many cases, it had been made to bear with prejudice and discrimination upon members of our profession."

According to Wey, physicians assume certain responsibilities when they freely choose to study and undertake a career in medicine, and assume the other advantages that go along with such a career. They are obligated to honor agreements they enter into with patients who seek their care, in the same manner as a lawyer or skilled tradesman; failure to do so could result in a charge of malpractice. Wey believed this was a fair method of considering the physician-patient contract. A physician is also not obligated to accept a patient if he does not want to, as lawyers and other skilled tradesmen may also refuse clients. However, Wey admonished his audience, once a physician chooses to accept a patient, he is strictly obligated to "exercise his best skill and all necessary diligence to carry it to a speedy and successful termination. He cannot abruptly terminate his connection with a case, without giving timely notice of his intention to withdraw from its care. Failing thus to give notice will subject him to liability for the consequences of his act, which is held to be a serious form of negligence." Yet, it was important to stress the fact that the physician-patient contract was not a guarantee of a certain result, unless specifically stated. "Unless a contract is made between a physician and his patient to accomplish a specific result, the former cannot in any manner be regarded as a warrantor or insurer."

The question of the individual physician's skill as it related to charges of malpractice was a perplexing issue to the physician of 1872. Precedent decisions of the day indicated that a physician of higher-than-average skill could not be held to higher accountability in malpractice cases because of his greater skill; Wey cited a Maine decision that stated the following: "This rule [referring to requisite skill and knowledge] does not require the possession of the highest or even the average skill, knowledge or experience, but only such as will enable [the physicians] to treat the case understandingly and safely. . . . A degree of skill below the average in a profession ceases to be skill and becomes ignorance, and it is not easy to perceive in what manner such imperfect knowledge can be accounted sufficient to treat the case understandingly and safely." This makes the ruling puzzling because under its constraints, it would be difficult if not impossible to prove malpractice in a skillful physician. However, according to Wey, "a skillful physician is expected, nevertheless, to devote to a case more than common skill, as skill is estimated among medical men as they are found in a community. The fact that he is employed in a case because he enjoys reputation and is conceded to possess superior knowledge, implies that he will not exercise common or ordinary skill, but the whole force and strength of his ability." A physician's skill also should be comparable to the level of the skill in the locality where he practices. These observations support the modern physician's statement that the most talented physicians are the ones who are sued the most often, because their skill and the level of skill in the hospitals in which they practice is so high that patients often expect extraordinary results.

Judgment was another gray area for the 19th century physician, according to Wey. Some decisions rendered the meaning of best judgment to be virtually synonymous with skill, diligence, and care; other decisions went against physicians who were proven in the courts to be eminently skillful, but guilty of malpractice because of errors in judgment.

Had physicians of the 19th century the opportunity to purchase malpractice insurance, the fee differences between the various specialties might have been quite similar to the disparities existing today. Wey noted that ". . . surgeons almost exclusively and physicians rarely have been held to accountability in the charge of malpractice . . . The allied character of anatomy and surgery, and the direct dependence of skill in the latter [and] upon knowledge in the former . . . renders the practice of this branch of science more precise and demonstrable than the interpretation of symptoms in the ordinary course of disease and the fitting employment of remedies." The result is that the surgeon "engages in a work of acknowledged re-

sponsibility, which subjects him to vexation and annoyance, from which his more fortunate neighbor in medicine is entirely relieved."

Exacerbating the 19th century physician's malpractice problems were 19th century lawyers. Wey pointed out that because of deficient education and relaxed requirements from the legislature for entrance into the legal field, unskilled lawyers bogged down the court system with improper suits, committing the same professional malpractice against their own clients that they charged in suits against physicians. The faulty legal practice held a high cost for the state, but lawyers rarely policed their own leagues, allowing fraternalism to obstruct the rights of the very clients they sought to protect. Wey asked, "Should one profession prey upon the other not because of superior knowledge, diminished liability, greater virtue or strength of purpose, but because it has control of the machinery by which the process of complaint of malpractice and efforts to convict under the charge, are made to bear with undiscriminating and hateful effect?" Wey continued: "But what shall be said of an attorney who advises a suit of malpractice against a physician and conducts its management in court, under an implied agreement that if he does not succeed in obtaining judgment, his services shall be gratuitously rendered; but if a verdict is found for his client, he will retain one-half or some other specified sum as his share of compensation! If such a course is not the most flagrant malpractice, it would be difficult to conceive of an offense that would justify a more pointed use of the term. It is more than malpractice; it is an attempt to extort money, by inducing a jury to believe that injury has been done to a client, that pecuniary advantage may accrue to his attorney. It is virtually, by the terms of the agreement entered into, placing the attorney in the position of the party on whom the alleged malpractice has been visited . . . the same obloquy should attach to an attorney who brings an action of malpractice against a physician with the expectation that it will not come to trial, but, for fear of expense and annoyance, will be settled by the defendant for such a sum of money as will prove satisfactory, not to the plaintiff, actually, but to his cunning and unprincipled advisor."

Aiding lawyers in the continuation of malpractice suits were two other factors, according to Wey—the "traitorous men"—physicians who testify against colleagues as alleged expert witnesses, and the juries deciding malpractice cases, "who are in no manner qualified, as juries are commonly composed, to decide in manners affecting the rights and responsibilities of physicians." Because of these factors, Wey believed, "Men of conspicuous ability have been driven from the profession through fear of being held to responsibility for the consequences of surgical practices . . . After years of faithful devotion to duty, and the realization of the products of toil and labor, with which to educate children or to comfort the decline of life, the inexorable verdict of a jury has despoiled such men of their goods and substance, and reduced them to penury."[6]

Physicians encountered other problems in the courts, such as statutes that favored plaintiffs in malpractice cases. Statutes at that time allowed patients to waive the right of confidentiality of physician communications in a selective manner. A plaintiff could allow an attending physician whose testimony would be favorable to speak, but by exercising his right could silence the testimony of other attending physicians whose testimony would favor the defendant. In an 1891 article, Wilding noted the following: "The decisions which give patients who have employed or been attended by several physicians the right to waive the privilege in regard to one or more physicians and not in respect to the others are in some cases manifestly unjust, and open the way for great injustice being done the members of our profession when dealing with unscrupulous and designing people."[7]

History of Malpractice in the *New York State Journal of Medicine*

From 1900 to 1909. The turn of the century brought a new awareness about the problems of malpractice suits, and the first organized efforts to address the problem. James Taylor Lewis, Counsel to the New York State Medical Association, in a letter to the editor of the *Journal* in 1901, called for the Council of the Association to develop a plan to afford members protection from malpractice.[8] However, the malpractice Lewis spoke of was not malpractice as it is known today. Malpractice to the early 20th-century physician meant blackmail: an unhappy or devising patient, in league with an unscrupulous lawyer and a physician who was willing to testify as an expert to benefit the plaintiff for a share of the settlement. Suits would be introduced or threatened against usually young, unestablished physicians, who would be so fearful of the effect of a malpractice suit on their reputations that they would agree to pay a settlement to the patient in order to avoid going to court. "Do we care five dollars' worth a year for the honor of the medical profession, the sympathetic supporting and succoring of a brother practitioner in his time of distress, and for person insurance against the expense of defending a suit against malpractice?" asked Quimby in a letter to the editor in 1901.[9] He suggested that the New York Association should set the standard for other states to follow as "the first to undertake the defense and support of its members, and to distinguish between the defense of honor and the compromise of blackmail."

By December of 1901, the Association had developed guidelines for a proposed malpractice defense system and published them in the *Journal* for member review.[10] The guidelines were as follows:

- The Council shall, upon request and compliance with the conditions hereinafter provided, assume the defense of suits for alleged malpractice brought against members of this Association.
- The Council shall not undertake the defense of any suit based upon acts prior to the qualification of the accused as a member of the Association.
- A member desiring to avail himself of the provisions of this article shall make application to the Council through the secretary, shall sign a contract renouncing his own and vesting in the Council sole authority to conduct the defense of the said suit or to settle by compromise, and shall make such other agreements as the Council may require.
- The Council shall thereupon contract with said applicant to take full charge of said suit, to furnish all necessary legal services, to pay all necessary expenses and not to compromise said suit without consent of the accused, but the Council shall not obligate the Association to the payment of any damages awarded by decree of court or upon compromise.[10]

DEFENSE OF Malpractice

SUITS IS GOOD

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New York State Journal of Medicine 1905; 5:xiii.

In 1902, the New York County Medical Society adopted an almost identical plan for the defense of its members from unwarranted malpractice suits, with the provision that the plan would be abolished when the State Association adopted a similar plan. "Timid and thrifty members will have no object in settling out of court, because it will be cheaper for them to fight than to settle," an editorial in the January, 1902 issue of the *Journal* read.[11] Participation in the program cost an annual fee of $5. It is notable that physicians realized that some malpractice suits did possess merit; the final paragraph of the editorial said the Association "does not for a moment intend to protect its members who have been guilty of actual malpractice further than to see that they get justice."[11]

Letters and newspaper editorials in favor of proposed guidelines for the State Association were printed in the *Journal* in 1902, and the guidelines were adopted at the Association's annual meeting in October of that year. According to an editorial published in the *Journal* in 1903, "It will take little time for the lay public to learn that members of the New York State Medical Association are poor subjects to attempt to frighten, as their legal defense is furnished gratis, but as soon as they learn it through the publicity given to a suit or two, the blackmailing variety of malpractice suits will cease. This class constitutes 97% of all such suits brought."[12]

From 1904 to 1906, malpractice remained an important issue for the Society. Counsel James Taylor Lewis wrote several lengthy articles concerning the Association's defense plan and its success in reducing the number of malpractice/blackmail suits. "The application for the defense has come from all parts of the State, and up to date there has not been secured a single dollar as a verdict against any member who has applied," he wrote in a 1904 article.[13] Another issue Lewis addressed in the same article was the solicitation of physicians by medical malpractice insurance companies. During this decade two insurance companies, The Fidelity and Casualty Company of New York and The Physicians' Defense Company, regularly printed advertisements in the *Journal* for physicians' liability insurance. In 1901, insurance with the Fidelity and Casualty Company cost physicians $10 per year. The Society was against the use of outside insurance companies for protection against malpractice because it was believed that companies would be more willing to settle a case out of court, thus making physicians easier prey for blackmailers. Lewis stated, "I believe that the contracts of most insurance companies should not be made use of by physicians, for the readiness to compromise following the threat of a suit tends to make his brother practitioner also prey of the shyster. Persistent fighting such as is afforded by the defense of the State Medical Association alone will stamp out this evil."[13] There seems to be evidence, however, that the insurance companies attempted to compete with the Society for enrollment in a defense plan. One Fidelity and Casualty Company advertisement of 1905 states, "Defense of malpractice suits is good, but the busy doctor also wants PROTECTION. The Fidelity and Ca-

sualty Company of New York defends its clients against any such proceedings at its own cost, and if damages are awarded will PAY them." This advertisement was directed at making the point that the Society's plan would not pay damages for the physician if a case were settled against him. The Society countered these advertisements not only in the columns of the *Journal* but also on the advertising pages; several full page advertisements were printed discussing the advantages of the Society's defense plan. Apparently physicians were more likely to choose the Society's defense plan, because the advertisements for the insurance companies ceased to appear after 1910. Possibly, the *Journal* stopped accepting the advertisements.

During this decade, a "Medico-Legal Bulletin" column also began to appear in the *Journal*, the first in June of 1904. The column discussed cases that had been settled in court and other questions of liability. One column was devoted to a discussion of physician's liability for neglect of a patient during vacation.[14] It seems that although the malpractice problems the physicians faced during the first decade of the 20th century were only marginally related to the problems of today, the questions of liability and protection from liability had become an issue of concern for physicians and organized medicine. From this point on, awareness of the problem never disappeared.

From 1910 to 1919. There is only one mention of liability in the *Journal* during this decade[15]; the onset of World War I in 1914 may have been responsible for diverting the attention of physicians to other topics. The one article is an editorial commenting on the question of the legal liability of hospitals. The discussion involved charitable institutions, which at the time were immune from liability for malpractice caused by one of the hospital's employees on one of the charity patients. In New York State, however, that immunity was only partial. A 1910 decision on the question of the liability of charitable hospitals ruled that the institution is only immune from liability if the victim of the malpractice received care through the charity of the hospital. If the injury befell a person who was not a charity patient, the hospital maintained full liability for the damages done to the individual. The judicial authority who provided the legal information for the editorial maintained that a similar decision would probably be rendered if malpractice occurred involving a patient who was a paying customer in a charitable hospital, because the relationship between the two parties would be contractual and not related to charity.[15]

From 1920 to 1929. Concern over malpractice increased during this decade. Twelve articles were printed in the *Journal* discussing many different aspects of malpractice; the topics indicate that malpractice suits were increasing, and were more often of a legitimate variety.[16-28] In 1921, the House of Delegates adopted a plan to supplement its defense of suits against members with an insurance policy providing coverage for physicians if a malpractice judgment went against them. This is the first time the Society sanctioned the use of any insurance for the purpose of malpractice claims. According to Sondhern, "the increased number of technical procedures involved in the modern practice of medicine have notably increased the physician's hazard relative to supposed malpractice. This is clearly apparent not only in the increasing number of suits for malpractice, but also in an analysis of the reasons why these suits are brought."[16] The Society had still been "almost universally successful" in the defense of suits against members, but the presence of the additional coverage would afford the physician peace of mind during the time of the trial.

The general counsels of the Society kept members informed of precedents set in court cases that affected malpractice suits. The information appeared in a "Legal" column that began in February of 1923. Particularly of concern to physicians at this time was the statute of limitations for malpractice suits, and the statute for suits for nonpayment of services. Physicians who sued patients for the collection of fees before the two-year statute of limitations for malpractice suits expired often found themselves a defendant in a counter-suit of malpractice, according to George W. Whiteside, general counsel for the society, in his 1923 article, "The Physician in Court."[19] Whiteside admonished physicians: "The claim of malpractice is outlawed in two years; your claim for fees earned is outlawed in six years. You, therefore, have four years in which to sue without the inconvenience or trouble of a possible or baseless counterclaim for malpractice." An article summarizing a court decision upholding the statutes of limitation appeared in the *Journal* in 1927, authored by Lloyd Paul Stryker, Esq, counsel for the Society.[26]

When a malpractice claim did go to court and liability was established, it was important for the physician to determine clearly the amount of the damage. Whiteside noted that if excessive claims were paid too frequently, the result could be an increase of the $18 per annum premium, or even the decision by the insurance company to stop writing this type of coverage.[19]

Much of the counsels' commentary and observation are still germane to the malpractice crisis of today. In a Whiteside legal column of 1924,[21] he commented on whether a physician is liable for malpractice as a result of the physician's selection of one accepted procedure over another with unfavorable results. "If the . . . method were a recognized approved method, it could not be contended that there is liability, because to do so would require that we hold that a bad result is evidence of malpractice. . . . It becomes a matter of judgment as to which procedure a physician should employ. If the profession is to be deprived of this freedom in the treatment of disease, no progress can be made. Departure, of course, from approved methods may be at the peril of the physician employing such. This may be the penalty that has to be paid for attempting innovation."[21] In a 1925 column addressing the problem of unscrupulous physicians who instigate malpractice suits against colleagues for profit, Whiteside suggested that steps should be taken "to place the responsibility for groundless actions upon those who are responsible."[24] In another article, Whiteside advised physicians that when a problem arose in their treatment of a patient "that the physician [should] at once advise the patient . . . or some responsible member of the patient's family or friend . . . that the accident has happened. . . . Endeavor in these circumstances likewise, to get consent before undertaking even a minor surgical procedure. . . . The observance of these simple rules of procedure will be a great protection to the physician against claims of exag-

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New York State Journal of Medicine 1905; 5:xiii.

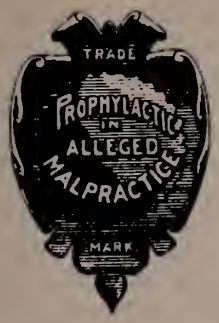
gerated damage by the patient and will prevent a false and sinister construction being placed upon the physician's silence."[18] In 1926, Lloyd Paul Stryker wrote an extensive article instructing physicians on the art of giving testimony in malpractice cases.[25]

The malpractice crisis of today, which many trace back to the malpractice problems of the early 1970s, might find Whiteside's comments of 1925 surprising: "Four years ago the medical profession in this state faced a crisis in meeting law suits brought by patients against doctors. . . . Some insurance companies that had written policies of protection against such law suits deemed it necessary to treble their rates. . . . Some insurance companies were abandoning entirely the writing of such protection." Whiteside encouraged Society members to join the indemnity policy the Society had established with the Aetna Life Insurance Company, and avoid companies trying to undersell the Society's plan. "Companies now doing the business below cost would have to make future rates sufficiently high to make up for the loss which they would occasion by such a practice."[22]

From 1930 to 1939. Discussion of malpractice during this decade was limited to five articles, addressing legal aspects of malpractice and malpractice insurance.[29-33] In a 1930 article, Lloyd Paul Stryker reported on a recent court case in which the definition of a malpractice suit was limited to cases involving physicians and surgeons. A lawyer defending a nurse who was accused of malpractice got her case dismissed because it was not commenced within two years of the occurrence. An appellate court reversed a decision of a lower court, holding that "the meaning of the term malpractice in the statute was limited to physicians and surgeons, and did not include actions brought against a registered nurse for claimed negligence in the treatment of a patient."[29]

Malpractice claims against unlawful practitioners were discussed in a 1932 article. In the case reported by counsel Lorenz J. Brosnan, a malpractice claim was brought against a chiropractor (the practice of chiropractics was not legal in New York at the time). The defendant tried to introduce evidence to the court exhibiting his skill in the field of chiropractics and illustrating that the treatment given to the plaintiff was appropriate in that field; the judge ruled that the evidence was inadmissible. "If he undertakes to practice medicine and he does so contrary to the law, he cannot escape civil responsibility for negligence, such negligence as a physician would be held for, by pleading either that he was not a physician or that he made a contract to treat the patient according to a distinctive system not recognized by the profession of medicine."[31]

At the 1933 House of Delegates meeting, the delegates revised and codified the regulations governing malpractice defense and group insurance. "From time to time, during the operation of the Plan, questions have arisen which required the adoption of rules by the Society to prevent unequal benefits flowing to a comparative small number of members at the expense of others," the report read.[32] The recipient of "unequal benefits" referred to physicians whose attitude or practice represented a potential



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New York State Journal of Medicine 1905; 5:ix.

threat to the Society's program. "When upon the final completion of the defense of any suit or claim it shall appear to the satisfaction of the Executive Committee that the medical procedure, conduct or attitude of the member involved was such that it could not have the approval of competent medical opinion generally and that the continuance of such medical procedure, conduct or attitude would constitute a burden to the Society's Group Insurance plan more hazardous than that contemplated in what is generally accepted as the competent practice of medicine, the Society shall have the right to withdraw from such member the privilege of renewal of his indemnity insurance under the plan." The Society's plan of 1933 did not cover liability stemming from the use of x-rays for therapeutic treatment; it also did not cover any liability stemming from the acts of partners, assistants, or nurses working for the insured party, or liability resulting from any practice or hospital in which the physician had a controlling interest, unless the liability was related to the insured physician's practice therein.

By 1939, the Society's needs had outgrown its original program. A lack of desired facets of coverage in addition to "an unwarranted rate increase request" led the Society to redraft its insurance program with a new company, the Yorkshire Indemnity Company of New York.[33] The new insurance program allowed physicians to select a broader form of coverage; reduced surcharges for excess coverage (for services such as x-ray therapy) in addition to the base charge for minimum coverage allowed the physician to increase his coverage if he so desired without great cost increase. Physicians could also choose to cover just one facet of their practice: for example, if a physician wanted coverage only for his work in x-ray therapy, he could pay only the cost of the surcharge for x-ray therapy coverage and limit his insurance to that area. Additionally, physicians were now also covered for liability incurred by temporary substitutes, permanent assistants, and licensed or specially qualified technicians, as long as those persons were members of the Society and also individually covered.

The new coverage agreement allowed the base coverage premium to be reduced to $28 per year, and was expected to save the Society more than $40,000 per year on the cost of coverage. The improved program "will not escape the consideration of prudent members who have watched with apprehension the growing size of suits and the tendency of all juries to return higher verdicts."[33]

From 1940 to 1949. "Each year showed an increase in the number of suits and claims filed against members throughout the state and similar increases were reported from other parts of the country. . . . The awards made by juries also rose sharply and the seriousness of the situation soon forced itself upon the attention of the entire profession. In this state, the astonishing increase in the number of suits filed and the cost of disposing of them was regarded simply as an abnormal run of chance that would flatten out when the unsettled conditions . . . returned to normal. But as time went on, the situation grew worse instead of

better."[34] This description may sound similar to the malpractice climate of the early 1970s or 1980s, but actually it is describing that of the early 1920s. The article was written in 1943, commemorating the 22nd anniversary of the Society's group insurance plan. Since its inception in 1921, "over 3,500 suits and claims have been closed by the companies operating under it, with the assistance of the legal counsel of the Society, and all liabilities have been fully discharged."[34]

Medicolegal columns reappeared in 1940 and 1941, discussing aspects of liability involving not only physicians but also institutions and other health care personnel. Of the other four articles that appeared during this period,[35-38] one discussed a decision physicians of today would rally behind. The case involved a woman treated for polio who sued a physician because she was unhappy with the results of a treatment method employed by the physician. The defendant and an expert witness provided by him testified that the procedure was proper, and that the results, while not entirely successful, were acceptable considering the treatment and the woman's condition. The woman did not produce any expert testimony to contradict these opinions; however, the jury returned a verdict in the woman's favor. The case was appealed to the Appellate Court; the judgment was reversed and the action dismissed on the grounds the plaintiffs had failed to establish their cause of action. " . . . The respondent was treated properly . . . and a bad result followed. A doctor is not to be charged with negligence because the result is not what is desired . . . a doctor is not a guarantor, and the mere fact that a bad result may follow an operation is not of itself evidence of negligence," the court's opinion read.[37]

From 1950 to 1959. The frequency and nature of articles that appeared during this decade indicate the increasing seriousness of the malpractice problem. The thoughts of physicians seem to have moved from eliminating the malpractice problem to trying to find a way of addressing the problem, which, for all the Society's efforts, had only worsened with time.

During this decade, the malpractice issue began to resemble more closely the situation that exists today, with more concerned parties involved. Authors of malpractice articles included officials of medical societies of other states, insurance company representatives, lawyers, journalists, and academicians. Also seen for the first time was displeasure among physicians over the Society's inability to keep the costs of its malpractice insurance program down. According to a *Westchester County Bulletin* editorial (quoted in a *Journal* editorial commentary), some physicians and county societies were considering negotiating with outside insurance companies for individual policies, because the Society's program was costly, and some physicians believed it did not provide adequate protection.[39]

"Who makes the group's premiums?" asked an anonymous voice in the commentary.[39] This question revealed the relative inexperience physicians of the 1950s had in dealing with malpractice insurance. Perhaps when premiums were lower and provided adequate coverage, physicians had no reason to ask that question. The situation had grown serious enough, however, for the *Journal* to reprint an article from *California Medicine* entitled, "What Price Medical Malpractice Insurance?"[40] in which California Medical Association official Joseph F. Sadusk attempted to answer the same question for its members who were experiencing similar problems. Sadusk noted the following: " . . . it is extraordinarily difficult for insurance carriers to predict losses with any accuracy for a given policy year, since the policy for the year in which the incident occurs is the policy which covers the physician for the rest of his life, regardless of the year in which the suit is filed," not knowing that in less than ten years, most physicians would be well-versed in the concept of the "long tail." "In the case of medical malpractice insurance, the calculation of premiums is extraordinarily difficult due to the factors of latent liability, inflation, an increasingly critical attitude of the public, and the generosity of juries in awarding higher and higher judgments."[40]

Malpractice decisions in the nation's courtrooms also served to put physicians on the defensive. In his 1959 article, "Is There a Doctor in the Courtroom?" lawyer R. Crawford Morris was less than encouraging.[41] "Some 5,000 cases are now being tried each year with thousands of other cases settled out of court. Since 1950, one out of every 35 doctors insured under the New York State Medical Society's group insurance plan has been sued in the courts for malpractice," Morris quoted from a *Newsweek* article. According to Morris' description, " . . . 2% [of malpractice cases] are what I call 'blood money' cases, where the patient or plaintiff was looking for trouble from the beginning . . . 3% are merited . . . 95% are unmerited . . . [arising from] a combination of two factors: first, an untoward result so that there has been considerable pain and suffering, and second, superimposed upon the first, poor public relations either on the part of the defendant doctor himself or quite often on the part of a subsequent treating doctor who on viewing a poor result unthinkingly exclaims, 'My heavens, who did this to you?' "

Also dangerous to physicians was the habit of courts to loosely interpret the rule of *res ipsa loquitur*, Latin for "the thing speaks for itself." This doctrine, Morris explained, was "originally limited to cases where the untoward result would not ordinarily happen unless the defendant was negligent and to cases where the defendant had exclusive possession and control of the instrumentality causing the injury and where there could be no contributory fault on the part of the patient. Some of our courts have extended this doctrine to include cases where the patient cannot explain what went on, whereas the doctor can, the dramatic example of this being of course surgery." This "perversion" of *res ipsa loquitur*, which Morris referred to as a "rule of sympathy," was most dangerous to physicians in cases arising from complications during surgery. "To apply the rule of sympathy to such cases is to hurl you into the lion's den of jury speculation, wherein you are judged, not by your fellow doctors who are fully aware of the medical facts of life confronting you during the operation, but by 12 lay citizens who can have no comprehension of such complicated medical facts, but who have a very great deal of comprehension and natural sympathy for the pain and suffering attendant on almost every untoward result."[41]

Such articles must have struck fear in many physicians, and surely led to evolutionary changes in the relationship

between physicians and patients. Morris' article and others gave advice to physicians on how to deal with patients in order to avoid a malpractice claim; the perception of patients as potential plaintiffs had begun.

From 1960 and beyond. With malpractice now firmly entrenched in the modern era, it became a popular topic in the *Journal*. Numerous articles appeared, addressing the malpractice problems particular to individual specialties, discussing insurance policies, citing malpractice case precedents, and instructing physicians on how to avoid suits or how to deal with them as they arose.

Some links with the past were severed during the 1960s and 1970s. An article written in 1960 reported on a 1957 Court of Appeals decision that removed the immunity of all hospitals, including charity hospitals, for malpractice committed by staff members on charity patients[42]; the previous time this law was discussed in the *Journal*, it had been upheld by a court in 1911. In 1973, 71 years after the program was initiated, the House of Delegates voted to end the provision of free legal defense for members involved in malpractice cases.[43] Soon afterward, one of the greatest blows in the malpractice fight was struck against physicians: malpractice carriers, citing tremendous financial losses, claimed they were unable to write malpractice policies without exorbitant increases. Finally, those carriers left the market, leaving physicians without a source of coverage. The Medical Society of the State of New York, as other medical societies around the country, formed its own insurance company: the Medical Liability Mutual Insurance Company. Few physicians (if indeed any) need to be told what has happened since. The articles cited here lend a historical perspective to what we often perceive as a modern problem. The malpractice articles written today continue to chronicle the history of an issue that was not only of major importance to the physicians of the past, but which also concerns physicians of today.

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Compensating for medical injuries

Is there an effective alternative to the tort system of medical malpractice?

LAURENCE R. TANCREDI, MD, JD

Approximately ten years ago a malpractice insurance crisis occurred, as demonstrated by insurance companies withdrawing malpractice insurance coverage for physicians and specialists in particular.[1] It is now apparent that a second major crisis in malpractice has developed. As reported recently, malpractice insurance premiums are on the increase (*New York Times*, January 15, 1985, p A1; January 17, 1985, p A1; February 21, 1985, p A14). It has also been reported that the largest medical malpractice insurer in New York had been granted a 55% increase in malpractice insurance premiums by the State Superintendent of Insurance (*New York Times*, April 5, 1985, p A10). The increase will affect 16,000 of the 22,000 physicians who are self-insured in the state. The average costs of medical insurance premiums for physicians will increase from approximately $4,000 per year in 1975 to $19,000 per year with this recent increase in rates. As would be expected, the rates for some specialists—especially surgeons, neurosurgeons, and obstetricians—who are also among the highest paid in the medical profession,[2] will be high in certain parts of the state.

During the 1975 crisis, insurance companies argued that they were unable to handle financially the requirements of insurance coverage for medical malpractice because of the increase in both frequency of claims and size of settlements. The average indemnity per claim increased from $10,000 in 1970 to $16,000 in 1975.[3] The occurrence of cases resulting in awards greater than $1 million has also increased. Statistics for 1982 to 1983 show that as many as 250 or more settlements resulted in awards greater than $1 million each (*New York Times*, February 4, 1985, p A18). Concomitant with this escalation of indemnity in the mid 1970s there was an increase in medical malpractice premiums. In the decade between 1960 and 1970 the premiums for surgeons increased 949%.[3] Insurance premiums for physicians other than surgeons and for hospitals also increased during that decade by approximately 540% and 262%, respectively.[3] Research by the California Medical Association revealed that the increase in individual physicians' premiums has been as high as 400% since 1970 (*New York Times*, February 4, 1985, p A18). Much of that increase occurred in the first five years of the 1970s, which led up to the decision by many insurance carriers in 1975 to either increase their premiums drastically or abandon coverage of medical malpractice altogether.[1] Between 1975 and 1983 the malpractice insurance rates in general for physicians increased more than 80%.[4]

The economic strains created by the increasing frequency and size of awards in medical malpractice caused a shift in focus to an assessment of the efficiency and effectiveness of the existing legal and administrative systems. For each dollar of premiums paid by the provider, the successful claimant receives a very small percentage. One study estimated that for every premium dollar, the proportion going to the patient is approximately 17%, the rest being consumed by preparatory and transactional costs associated with civil litigation.[5] A more realistic estimate would be roughly 56% of each dollar being received by the successful claimant and approximately 44% absorbed as legal and other direct fees.[6] The transactional costs are reflective of the contingency fee system as well as the consumption of time of highly trained personnel that must go into the preparation of a case and the actual time spent in court. This is to assure that the process is as fair as possible. Even so, a disproportionate amount of each dollar is utilized for expenses other than direct coverage of the patient's losses from the injury incurred in the medical care system.[7]

A review of claims to determine the degree of compensation received by successful claimants has shown that those persons incurring the greatest injury are most often paid indemnities that represent no more than one half of their losses. In contrast, claims made under $10,000 are likely to be compensated by a factor of four to five times the amount representing medical care expenses, loss of wages, and possible functional loss.[6] With regard to the small claims, the difference is probably reflective of some factor representing pain and suffering. From those losses totalling more than $100,000, pain and suffering, which is often alluded to as one of the major reasons for inflation of the cost of medical malpractice, seems to be of negligible influence as the patients are receiving less than they need for coverage of their losses alone.[6] These figures represent approximations of the relative differences in high versus low awards with respect to compensation for actual losses. The information on losses in the closed claim study from which these data were derived was not always complete, so that the actual losses may be underestimated rather than overestimated.

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Over and beyond the discrepancies in the amounts of money received through premiums versus those distributed to successful claimants, the existing malpractice system exhibits other structural difficulties. In the 1973 report of the Secretary's Commission on Medical Malpractice,[8] a survey was presented that disclosed that a claimant has less than one chance in eight of successfully convincing an attorney to take his case. In large part, the contingency fee, which creates incentives on the part of the lawyer to take cases that are most likely to be successful and have significant awards, works to the disadvantage of claimants whose claims may not be of sufficient size or who do not have as likely a chance of success. The National Association of Insurance Commissioners' (NAIC) study disclosed that even in those instances where lawyers are willing to take cases, approximately two thirds of the claims are resolved with no payments to the claimants.[6] The study also disclosed that 90.2% of claims are settled out of court. Of the 7% that actually go to trial, approximately one quarter come out in favor of the patient.

More recent statistics from the NAIC's survey of claims that closed between July 1, 1976 and June 30, 1978 showed a significant increase in the number of claims that actually got to trial.[9] This study disclosed that 16% of cases go to court, in contrast to only 7% in the earlier study. From another perspective, however, physician-owned companies are proving to be more formidable as opponents in the courtroom scene, winning about 90% of the cases as compared to approximately 80% a few years earlier.[9]

In addition to issues relevant to the financial and accessibility considerations of the tort system, there are other serious problems that have not yet been resolved. When provided, compensation for the successful claimant is relatively unpredictable. The losses are frequently undercompensated, as demonstrated by the NAIC data, particularly for awards greater than $100,000; in some cases they are overcompensated, where injuries that are not particularly troublesome may result in exceptional awards. Furthermore, by allowing for a third-party to intervene between the physician and patient, professional liability insurance may actually attenuate incentives for the avoidance of injuries. The physician, when subjected to a claim by an injured patient, need simply hand the data over to the professional insurer.

Besides these effects, the tort system creates some unfortunate consequences for the medical practice. Many physicians in high-suit specialties have changed the nature of their practice or have gone so far as to move into jurisdictions where suits are less frequent and awards of a smaller amount. Lastly, compensation for injuries in the tort system hinges on proof of fault or negligence by the provider. This results in eliminating all other medical injuries from compensation. The more critical focus of concern, however, should be on medical injuries generally, rather than just those that result in successful suits for the claimant because they meet the legal requirement of negligence and malpractice.

From the standpoint of the economics of the system, one of the most troublesome results of the tort system is what is referred to as the practice of defensive medicine. There have been no good studies on defensive medicine. It is a complicated issue to research, partly because it is hard to know what good medical practice is and whether any specific defensive activity is beneficial for the patient. Physicians and patients lean in the direction of using new diagnostic and treatment methods under the assumption that they are going to be more advanced and, therefore, more effective. New technologic developments such as coronary artery bypass surgery or computed tomographic scans shape consumer values and expectations and have a major effect on the nature of medical practice.[10] In a report by the Health Insurance Association of America, it was suggested that the fear of malpractice suits may create an annual inflation of as much as $3 to $6 billion.[11] Recently the American Medical Association estimated that the practice of defensive medicine may cost as much as $15.5 billion annually.[4] However, it has been suggested that defensive medicine and malpractice are being inappropriately portrayed as the cause for the ever-expanding costs of medical care in this country.[12] Although a good deal of what has been considered the practice of defensive medicine may be mythical,[13,14] many physicians nonetheless allege that the escalation of tort claims has resulted in a significant impact on medical decision making and the utilization of particular diagnostic measures. Although these perceptions may be exaggerated, they cannot be totally ignored for there has been growing concern among providers of health care to the possibilities of malpractice suits.

During the past eight years, several attempts have been made to shore up the tort system of medical malpractice. Some states have set ceilings on the amount of awards that claimants may receive in a successful action. Some of these have held up in various states[7]; however, in other states they have been successfully challenged in the courts as arbitrary and, therefore, violating the constitutional rights of the plaintiff.[7,15] Other states have enacted laws to decrease awards by the amount of collateral recovery, thereby minimizing[16] overcompensation for the individual's loss. Several states have modified the statute of limitations, decreasing the tolling period so that less time would be available for potential plaintiffs to initiate malpractice actions.[7,17] None of these approaches seems to be satisfactory. Although there are certain advantages to the tort system, such as the emphasis on the substantive due process rights of individuals who gain access to it, the control of prejudicial or unreliable testimony by formal rules of evidence which do not apply in alternative systems (eg, arbitration), and the impartiality created by a judge and jury, it remains inefficient in achieving its expected goal—the compensation of injured patients for negligent actions and the creation of a system that will emphasize avoidance of injuries through deterrence.

Alternative Approaches

The issues posed by the inadequacies of the tort system have led to a reassessment of exactly what is to be achieved by a system for redress of medical injuries. In the late 1970s, the Institute of Medicine (IOM) of the National Academy of Sciences set up a committee to review the problems of medical malpractice.[1] In the report of the committee three major goals that should underlie any effort to change the malpractice situation were described.

First, a system of medical redress should provide fair and equitable distribution of compensation for any loss associated with medical care. Secondly, it should be constructed so as to conserve resources by effectively reducing injuries. This might be achieved through a system of incentives for the avoidance of untoward outcomes. The third goal should be efficiency in the distribution and availability of resources to all injured patients. Of these goals, the two that appear to be basic to an ideal system of redress for medical injuries would be the prevention of injuries through injury avoidance and widespread compensation for losses.

The various systems that exist for handling medical malpractice and compensation for patients may be evaluated in terms of these three goals. On the one end of the spectrum is the tort or fault system, which includes innovative administrative alternatives such as arbitration and screening panels. On the other end of the spectrum is a program of compensation similar to the social insurance system. The tort system compensates only for those injuries in which it is possible to establish provider negligence. The social insurance system, in contrast, would compensate virtually anyone who became injured through the health care system. Though different in the nature and scope of compensation that is made available, both of these systems emphasize compensation over injury avoidance.

Somewhere in the middle of this spectrum is a third alternative—a designated event system. Such a system would involve identifying certain events that would be considered avoidable, and which would trigger automatic compensation when they occur. This would result in widespread compensation of those injured. In addition, by creating a list of designated injuries, the profession will hopefully begin to consider strategies for the avoidance of injuries in their treatment approaches.

Medical Injuries

The IOM committee focused on the complicated issue of medically-related injuries.[1] It concluded that this issue deserves serious investigation since actual negligence as understood in the tort system contributes only a small part of the adverse outcomes in the hospital care of patients. A basic question posed by the committee was whether or not all injuries, both avoidable and unavoidable, should receive compensation. In its report, the IOM committee took a strong position emphasizing the importance of collecting data on medical injuries generally. Since 70% or more of medical malpractice cases are hospital-based,[1] most of the studies that have been done with respect to determining the incidence and prevalence of medical injuries have focused on injuries occurring in hospitals. However, these studies may only be touching the tip of the iceberg with respect to the incidence and prevalence of medical injuries in the hospital.

A study by the California Medical and Hospital Associations conducted in the mid 1970s is perhaps the best known study dealing with medical injuries.[18] This study involved a review of 21,000 hospital records. Three physician-lawyers examined the records to determine the incidence of medically-related injuries. They discovered a rate of injuries of approximately 4.65% of all hospital admissions. However, only 0.8% of the records representing approximately 1,155 events indicated clear incidences of provider liability according to prevailing legal principles.

A second study that is often cited involved 800 patient records from two urban hospitals.[19] This research determined that injuries had occurred in nearly 8% of the cases reviewed. Finally, a third study involving 400 hospital records identified approximately 45 medically-related disabilities.[20] This represented an incidence of approximately 11%.

There have been two studies that revealed the wide scope of medical errors that occur in hospitals and the tort systems' relationship to them. The first of these involved a survey of avoidable adverse outcomes secondary to colonic surgery.[21,22] Approximately 56 types of errors were prescinded in this study of which 31 were related to contraindicated, unnecessary, or negligent surgery. The consequences of the adverse outcomes for these misadventures were quite severe. Twenty patients died in the hospital; of these 11 deaths were due to error. Of all the patients studied, only 31% (11) achieved a satisfactory outcome. Furthermore, the authors determined that the cost for treatment of the 36 injured patients was approximately $1,700,000, and the average hospital stay was 42 days. The researchers concluded that there are many severe iatrogenic events in this type of surgery that could be due primarily to an error in physician judgment. This judgment might have been rectified by better data collection and communication among those involved in the surgical procedure.

The second study involved monitoring 815 patients during a five-month period in 1979 on the general medical services at a university hospital.[23] About 290 or approximately 36% of these patients suffered one or more iatrogenic illnesses, and approximately 76 or 9% suffered major complications. Fifteen patients in this study died, representing approximately 2% of all the patients, or more significantly, 5% of those who suffered complications. It was believed that iatrogenic illness contributed more or less to the deaths of these patients. The authors of both of these studies emphasized the need for more effective methods for retrieving information regarding the hazards of hospitalization and for assessing the frequency and severity of iatrogenic events so as to create mechanisms for reducing their influence in the care of patients.

In addition to inadequately handling medical injuries, there are other important shortcomings of the tort system of liability. First is the capriciousness of jurors, or essentially their inability to evaluate medical responsibility. Secondly, compensation often does not depend on the scientific relationship between a medical intervention and a patient's outcome. Third, success in a legal dispute for the plaintiff as well as for the physician depends on the attorney that is hired for the case. Lastly, the tort system of compensation does not provide adequate compensation to the majority of those who are injured, not even from the standpoint of covering medical care expenses and loss of wages.

With regards to arbitration, there does not seem to be much data available at the present time. However, this system has been operating in hospitals like the Roos-Loos Group where it appears to be a viable alternative to the

tort system with its courts, jury, and judges. Proponents argue that once it is put into widespread operation it will offer savings in time and expenses in settling disputes.[24] This is somewhat questionable, although it would seem that with the relaxation of formal rules of evidence and procedures there would be some time and cost savings. The results from the National Association of Insurance Commissioners' closed-claims studies do not support this conclusion regarding cost savings.[6] Yet, one study has suggested that there is as much as a 13% decrease in the amount of time it takes to resolve cases that come before arbitration as opposed to the court system.[6,24] It has also been claimed that arbitration makes a better stab at understanding the scientific nature of medical injuries because the arbiters become increasingly knowledgeable about medical care issues. Furthermore, arbiters would not be as likely to be influenced by competing considerations as a jury might. Until a few years ago the Roos-Loos medical group in Southern California, which has had an arbitration system for about 50 years, had less than 10 cases arbitrated, even though it was mandatory in their plan for subscribers.[25]

There are disadvantages to arbitration. It is a relatively private procedure and, therefore, may have little effect on injury avoidance. Also, the relaxation of procedures and evidentiary rules in arbitration may erode the protection afforded by due process and the substantive rights of the parties. Finally, in time the arbiters may identify with the values of the providers of care, perhaps at the patient's detriment.

Screening panels provide another alternative under the fault system. However, unlike litigation and arbitration, there is a general lack of finality with the decision. After the case is decided by the screening panel, it may still end up in court. There is an exception, however, in Maryland. There the decision of the screening panel is converted into a legally binding judgment.[26] This was achieved through the passage of a law; it is currently the only state that converts a screening panel decision into a legally binding judgment. Generally, screening panels provide only one step in the tort process and seem to have a relatively poor record of accomplishment. They may actually slow down the system, and, therefore, are relatively inefficient.

In a review of mediation appearing in the *National Law Journal*,[27] several examples of difficulties with this system that highlight its inefficiency were provided. The article pointed out that from the inception of malpractice screening panels in Pennsylvania in 1976 to the publishing of the article in 1980, of the 3,000 malpractice cases submitted to them, only 14 had actually been heard. In 1981, these panels were abandoned in Pennsylvania. Other states, such as Florida and Missouri, had similar problems. The panels slow the process of decision making, adding to the time consumption and costs that are already problems in the existing tort system. Informality of rules of evidence, as with arbitration, also exists and in many states there is a question of the admissibility of the panel decisions at the time of trial since these decisions might unduly influence juries. Because of these reasons screening panels are not proving to be a viable adjunct to the tort system of medical liability.

What about social insurance as a possibility? A social insurance program would compensate everyone who is injured in the medical care system whether in hospitals or elsewhere, at least to the extent of their loss of wages and their medical care expenses.[1] This would certainly meet the goals of a widespread compensation system. And to the extent that a national health insurance system is possible in the future, the medical care expenses associated with injuries in the treatment context would likely be covered. However, social insurance would provide little incentive for the provider to avoid injuries,[1] unless it were linked to some regulatory body like a Professional Standards Review Organization (PSRO) or licensing agency.

Designated Compensable Events and No-Fault

The last of the alternatives discussed is a designated compensable events (DCE) system. The IOM report recommended that additional work be done on the feasibility of a DCE system.[1] Preliminary efforts to achieve this were taken by the American Bar Association's Commission on Medical Professional Liability,[28] but for the most part, research has come to a halt. This may be because there has not been a crisis in medical malpractice insurance coverage since the mid 1970s. On the other hand, given the cyclic nature of crises in medical malpractice, this would have been the most appropriate time to investigate the feasibility of alternative systems. Many medical malpractice lawyers claim that there has been a steady increase over the past several years in the frequency of suits and the extent of injury claims. Despite these signs, minimal research has been done to assess even basic issues such as the nature of medical injuries, when and where they occur, the extent to which they are preventable or treatable once they have occurred, and the advantages and disadvantages of various systems of compensation for the aggrieved patient.

In discussing the DCE no-fault system, it is important to place it into the context of other similar programs for medical injury compensation. The no-fault idea is by no means a new one. In the early 1960s, Professor Ehrenzweig[29] at the University of Chicago recommended that patients should receive compensation for all untoward events that occur during the course of hospital care. He explicitly excluded from compensation occurrences that might be expected to result from the disease condition that was responsible for the hospitalization. Unfortunately, he never fully defined such accidents or the nature of the adverse outcomes. From that standpoint, it seems that his system is almost comparable to a social insurance system. He provided no guidelines for making distinctions between the regular risks of life and those risks that are related to treatment or to medical care. Nonetheless, it was an important paper because it essentially introduced for the first time the idea that such an approach has possibilities, and that we could conceivably construct an alternative system for dealing with patients who are injured that might be more equitable in covering losses for injured patients, enhance the quality of care, and at the same time avoid many of the administrative or transactional expenses that are characteristic of the tort system.

Two no-fault proposals emerged in the 1970s that went a few steps further, and yet supported the overall thesis of

Professor Ehrenzweig. Both proposals defined certain types of compensable events. The first system involved Medical Adversity Insurance (MAI),[30] the other outlined an elective no-fault plan.[31] MAI provides a system of compensating patients based on the occurrence of designated compensable events. A group of specialists from each discipline are called together to look at a list of possible adverse outcomes and on the basis of a consensual agreement, determine those that should be considered compensable medical injuries in an automatic system of compensation. Elective no-fault[31] allows the health care provider, physicians or hospitals, to decide which outcomes or injuries they would be willing to compensate in the event that they should occur. This proposal was recently modified to suggest that health care providers arrange for their insurers to offer post-accident insurance to pay the net economic losses of an injured party. This offer, if accepted, would require that the injured person release his malpractice claim. This modification has been recently incorporated in the Moore-Gephardt strategy, which is a bill currently being considered before the United States Congress.[32] The elective no-fault system leaves the decision completely up to the individual physician. As a consequence, there might not be very much uniformity. One might decide on events A, B, and C, whereas another physician might decide on events X, Y, and Z. In the MAI system, designated events that are of particular significance to each specialty would be agreed on by all physicians who practice in that specialty. This would provide an opportunity for information feedback to the profession on the nature of what injuries are occurring, the quality of care that is being provided, and the ways in which such injuries may be avoided.

Two perplexing difficulties in designing a no-fault scheme are determining how events are to be delineated and adopting an appropriate causation assumption. When analyzing medical injuries it is difficult to pinpoint causation in the precise way that it is done in the legal system. Causation does not have a simple one-to-one relationship in medicine[33] as it might in the more exacting natural sciences. An exception, perhaps, might be in the case of an egregious error by a physician (ie, leaving a foreign body inside of a patient). Otherwise it is hard to sort out the nature of cause and effect and what the intervening physician or hospital did in relation to the injury that has developed. An alternative view, suggested by formulators of no-fault approaches, would focus more on an epidemiological or statistical pattern of causation rather than a traditional pattern.[33] Often there are a series of events that cumulatively result in a medical injury. Nonetheless, it may be possible to single out a particular accident-prone behavior of the providers that, if modified, would statistically decrease the incidence of the injury. This is substantially different than saying that there is a direct relationship between what a provider does and the occurrence of an injury in any one instance. This statistical notion of causation was developed by Professor Guido Calabresi at Yale Law School in his landmark book, *The Costs of Accidents*. This book analyzes the underpinning of a no-fault system and examines the question of what the compensation system may do to influence the actions of risk-bearers,[34] or providers of care.

The major stumbling block to all of these no-fault proposals has been that of designating compensable events in medicine. This is a very complex problem. In 1977 to 1979 the American Bar Association sponsored and published a feasibility study on designating compensable events.[28] The purpose of this study was to examine the conceptual basis of an automatic system of compensation, specifically to define and circumscribe adverse outcomes in a manner that would alert practitioners of their occurrences, as well as to inform patients of what constitutes injury, so that they could be appropriately compensated for their losses. The principal investigators of this study, two physician-lawyers, had both been involved in research in related areas. They focused primarily on two specialties—orthopedic surgery and general surgery—and relied on three data systems for identifying designated compensable events. The National Association of Insurance Commissioners had set up a study of closed claims for the period of 1975 to 1976.[6] This study has been extended to subsequent years, but the investigators only had data available from the 12-month period between 1975 to 1976 involving approximately 24,000 closed claims. More than 90% of the total malpractice claims that closed in the United States during that period of time were represented. Data from the California Medical and Hospital Associations' study[18] were closely studied, as well as data from a DHEW study.[35] Since the number of claims involved in the NAIC study was much greater than the combined claims of the DHEW and California Medical and Hospital Associations' studies, the NAIC data served as the primary basis for examining the extent and nature of medical injuries, some of which might be classified as designated compensable events.

In addition to establishing the feasibility of designated compensable events, this study by the American Bar Association also concerned itself with epidemiological information on the frequency, economic impact, and severity of the events. Particular importance was placed on those adverse outcomes that created the greatest financial burden, because such events had the most significant impact on the degree of indemnification sought through the tort system and the overall cost of health care. From a computerized listing of events that met the frequency, severity, and economic burden criteria, a number of outcomes were gleaned that could be considered potential designated compensable events. These events were easily detectable and clearly demarcated from other events that might confuse and distort the precision of the particular designated compensable event. A tentative listing was devised, which consisted of 25 financially burdensome adverse outcomes for general surgery and 24 for orthopedic surgery. These two listings were sent respectively to a group of consultant general surgeons and consultant orthopedic surgeons.

Once the panels were formed they were charged with examining the tentative listing of adverse outcomes and ranking them in terms of degree of relative avoidability, predicated on the preventability of the adverse outcome and whether something could be done immediately in the way of treatment to avoid long-term disabling consequences. This concept of avoidability is a statistical notion based on examining medical injuries in the aggregate as opposed to each injury individually. Events would be con-

sidered adverse if they resulted in additional medical care expenses or loss of wages for the patient. In addition to the medical considerations of avoidability, which include the ability to detect the adverse outcome, the panels of specialists were also requested to assess broad policy consideration, such as what the range of detrimental effects would be should the specific outcomes occur in a designated compensable event system.

On the basis of these broad criteria, the general surgeons agreed on 18 of the 25 adverse outcomes listed in the tentative listing and the orthopedic surgeons agreed on 15 of the events in their tentative listing. Some of the outcomes were easy to classify fairly accurately, such as the presence of foreign bodies unintentionally left in an operative site. Others were more complicated because they inevitably included in their definition both a description of the injury as well as the cause. For example, an item on the final listing of adverse medical outcomes in general surgery is serum hepatitis resulting from blood transfusions received during a surgical procedure. It is clear that the cause or the actual physiological process is incorporated in the definition of that adverse outcome. This is done intentionally to narrow it to an outcome that relied on a particular surgical setting and that could be agreed on by the surgeons. This would also assure that the event would be acceptable to the practitioner in the community.

One of the special features of this system is that it allows the opportunity for continuing assessment of adverse outcomes and for adding to the listing of DCEs. Surgeons and other medical specialists can develop a review system whereby they determine the appropriateness of adding particular adverse outcomes to a listing for automatic compensation. In addition to the importance of relative avoidability as a primary criteria for inclusion of these adverse outcomes in a listing of DCEs, there would also have to be some understanding of a *minimum threshold of significance*.[18,34] This would require that the adverse outcome cause a certain level of damage and result in either some increase in the number of days that the patient would need to be in the hospital, or a loss of a certain amount of wages. By requiring a minimum threshold the system provides for the means to eliminate the very small claims that would be insignificant in terms of their impact, but would create considerable administrative difficulties. Though there is arbitrariness on how the minimum threshold of significance is determined, it does allow for the opportunity to calibrate what adverse outcomes should be included in the system. For example, once the lists have been compiled the system may be found to be too expensive to compensate all of the people who would qualify. One way to limit the numbers of people compensated automatically, and thereby the number of events, would be to eliminate some of the adverse outcomes that have the most problematic statistical relationships of causation and relative avoidability.

The American Bar Association's feasibility study is a first step in the development of an automatic system. The importance of such a system is that it relies more on medical injuries than negligence as a way of determining inclusion for automatic compensation. In many ways this is still a theoretical notion, and it may not work or be efficient in practice. It has never been tested in a hospital or in any jurisdiction in this country. As a result, more research is needed, principally along two lines. First, the notion of formulating designated compensable events should be applied to additional specialties that have particularly high incidences of medical malpractice litigation. Obstetrics and gynecology, neurosurgery, cardiovascular surgery, and anesthesiology qualify as specialties with high incidences of adverse outcomes. These specialties were high ranking both in terms of cost and frequency in the study of the claims from the NAIC data.

After delineating lists for each of the specialties, an epidemiological study should be conducted in approximately 20 hospitals. The study would involve training clinicians to detect DCEs in order to determine the incidence and prevalence of these outcomes and their potential cost impact. This has already been done, to some extent, in California under the sponsorship of the California Medical Association. Dr Don Harper Mills, one of the chief investigators of the Medical Injury Study co-sponsored by the same organization,[18] has trained teams of clinicians (especially nurses) to detect adverse outcomes that afflict patients (personal communication, 1978). The clinicians examine hospital charts and evaluate patients to determine whether adverse outcomes have occurred. The patients often do not even know that they have been injured.

It has been argued that if every person who develops a condition that has been listed is compensated automatically, more money will be paid out than is through the tort system, despite the reduction of transactional and administrative costs. This may or may not be true. There is no empirical information, except retrospectively through the NAIC study which only dealt with claims that actually had been made as opposed to the whole universe of possible medical injuries. It will be important to develop an epidemiological study that will determine how often medical injuries occur in the course of a year, the severity or impact of such injuries, and the insurance implications should they be compensated.

The economics of the system is of vital importance. It may turn out that a DCE system would be more costly than the present tort system. By the same token it may turn out that once these events have been designated, provider behavior will be influenced so that physicians and health personnel will create fewer injuries. At least this will be a beginning of a framework on which to examine what health professionals have been doing in the medical care system.

Conclusion

The tort system of malpractice, including screening panels and other intermediary devices, is inefficient. If compensation is emphasized then it is clear that a social insurance system that would compensate all injuries would succeed most effectively to that end. However, such a system would be put into place at the expense of creating incentives for the avoidance of injuries, as there would be no effective means to bring about changes in the behavior of health care providers. The American Bar Association's commission study emphasized the need for incentives that properly align the behavior of providers so as to minimize and as much as possible eliminate the occurrence of medical injuries that are disabling to patients.

From the conceptual perspective, as pointed out in a recent journal article,[36] a no-fault system, in particular one based on designated compensable events, seems to meet some of the critical goals of tort law (accident avoidance, compensation, efficiency) in many ways better than the tort system itself. There would be minimal need for defensive medicine practices under the designated compensable event system. These practices are not only highly expensive in the ever-rising cost of health care, but create the possibilities for untoward outcomes, particularly where invasive procedures are involved. Secondly, a designated compensable event system would feed back to the profession specific outcomes that are highlighted to be avoided in the care of patients. It would also be a more efficient system bringing about lower transaction costs and relatively timely compensation to the injured victim. In this sense it would be an advance in terms of justice and utility with respect to the overall operational goals of a malpractice system.

There are still many unresolved issues that must be considered before a designated compensable event system can go into operation and be tested in actuality. Considerably more information is needed regarding the incidence and prevalence of outcomes that would fit the classification of designated compensable events. Events in each of the specialties need to be defined and actuarial assessments have to be conducted based on incidence and prevalence of injuries in order to arrive at the overall expense of compensation for medical care costs and loss of wages. Actual testing of this should also disclose the extent to which boundary issues emerge as to whether specific injuries fit within classifications that are designated. If they do not fit within a designated compensable event the patient will not receive automatic compensation, although he or she has the right to resort to the tort system. Boundary issues regarding classification of compensable injuries, as has been discovered in workmen's compensation, may be critical in terms of the overall effectiveness of the system. However, until a pilot project of implementation of a DCE system is put into effect, the full extent of this problem will not be known.

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An overview of medical malpractice legislation

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In a report published in the *Journal* in 1981, extensive data were provided on medical malpractice legislation enacted in the United States between 1971 and 1981 (1981; 81: 1814–1820). The information presented here has been updated to August 1985. The data and information were collected from the American Medical Association, several major liability insurers in various states, and from the Divisions of Governmental Affairs, the Executive Offices, and the General Counsels of the various state medical societies.

The pace of tort reform legislation in various states has recently quickened in response to the escalation of the liability crisis. Thus statutes may have been enacted subsequent to the tabulated information that follows.

EXPLANATION OF STATUTES

Ad damnum. This clause is the part of a plaintiff's pleadings that states the amount of monetary damages and other relief requested by the plaintiff in a court action. In medical malpractice actions (and in personal injury actions as a whole), this amount can often be an inflated figure that may not reflect the actual amount of damages sustained. Damages in such actions are often difficult to ascertain due to the intangible "pain and suffering" damages that often form part of the claim.

Advanced payments. Plaintiffs in medical malpractice actions often encounter financial difficulties as a result of illness, incapacity, or the loss of a spouse. In such situations where some liability is apparent, often the defendant's insurance company will advance to the plaintiff certain amounts to help alleviate the economic hardship, with such amounts to be offset against any award or settlement the plaintiff ultimately receives.

To encourage advanced payment practices, a number of states have enacted legislation to provide that any such payments advanced by the defendant or the insurance carrier to or on behalf of the plaintiff in a medical malpractice action prior to final judgment or settlement do not constitute an admission of liability for injuries or damages suffered by the plaintiff. Often such statutes also specifically provide that any advancements made to or on behalf of a plaintiff reduce any financial judgment or settlement by the amount advanced.

Arbitration. This relates to a voluntary procedure whereby patients and health care providers may enter into written agreements for the submission of any medical malpractice claims to binding arbitration. This procedure is an alternative to and in lieu of trial by jury and is not merely a condition precedent to trial. Furthermore, this procedure provides for limited judicial review of the arbitration decision instead of the complete trial on the merits in any subsequent court review.

Medical malpractice claims may currently be arbitrated in at least 30 states under the general arbitration statutes in those states. However, this report covers only those states that have enacted arbitration legislation specifically for medical malpractice claims. All of the statutes generally provide that a person's right to treatment shall not be prejudiced in any way by his or her decision either to enter or not to enter into an agreement for arbitration of medical malpractice claims. In other words, the agreement must truly be voluntary in order to be binding.

The statutes usually provide for an informal hearing before an arbitrator or a panel of arbitrators where the rules of evidence, which would be applicable in a court of law, are not strictly adhered to.

Attorney fee regulation. The most common arrangement for payment of plaintiff attorney fees in medical malpractice cases is the "contingent fee." Under this type of arrangement the attorney receives as his fee an agreed upon percentage (commonly 30% to 50%) of any final award or settlement made to the plaintiff (generally after the legal expenses such as filing fees, expert witness fees, and travel expenses have been deducted). However, if the plaintiff loses in court, the attorney does not receive any compensation.

Legislation enacted within the last couple of years regulating plaintiff attorney fees has taken two different courses. One course legislates a sliding scale for contingent attorney fees, most often expressed in terms of a percentage of the award. Under this arrangement, as the amount of the award increases the percentage permitted as contingent fees decreases. The other course provides that the court review an attorney's proposed fees and approve what it considers to be "reasonable fees."

Awarding costs, expenses, and fees. A few states have enacted legislation designed to deter the pursuit of frivolous medical malpractice claims. These statutes generally provide that where one party to the action has been found to have acted frivolously in bringing the suit, he may be found liable for payment of the other party's reasonable attorney and expert witness fees in addition to court costs. These statutes differ from the usual civil trial situation

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where court costs may be awarded to the victorious party, but in which payment for attorney fees and expert witness fees are normally sustained by the party who incurs them.

Burden of proof. The burden of proof is that which is required to be met by the plaintiff in order for him to prevail in his cause of action. Several states have enacted provisions relating to the burden of proof in medical malpractice cases, either by providing that the plaintiff must prove that the defendant has breached a particular duty of care, or by modifying that state's *res ipsa loquitur* doctrine.

Caps on physician's personal assets. Some states have enacted legislation that functions to limit physician liability in medical injury lawsuits, often by placing an absolute cap on physician liability under a patient compensation fund. In some states, a prerequisite for the physician to be covered is to meet specific requirements of that state's patient compensation fund. Some patient compensation fund statutes set a maximum on fund liability. In states with such fund maximums, the health care provider remains liable for any portion of a judgment or settlement above the fund maximum, unless there is also an overall cap on awards corresponding with the fund maximum or a limit on physician liability.

Certificate of meritorious claim. Medical malpractice complaints must be accompanied by a certificate executed by the plaintiff's attorney stating that he has reviewed the case, has consulted with a physician, surgeon, or dentist whom he believes is reasonably knowledgeable in the relevant issues, and that the attorney has determined there is reasonable and meritorious cause for filing the action.

If the attorney is unable to obtain consultation before the action is barred by the statute of limitations, then a statement to that effect must accompany the complaint. In such cases, the required certificate must be filed within 60 days of the complaint being filed.

Channeling of medical malpractice insurance by hospitals. Several states have enacted legislation that permits hospitals to purchase medical malpractice insurance to cover potential liability not only of the hospital and its employees, but also physicians on the medical staff.

Collateral source provisions. The collateral source rule is a rule of evidence that prohibits the introduction into evidence at a trial of any indication that a patient has been compensated or reimbursed for his injury from any source other than the defendant, such as private health insurance or workmen's compensation. Since this type of evidence is not presented to a jury, the plaintiff may receive double compensation for the same injury. (It is thought by many people that this situation often creates a windfall for the plaintiff and inflates malpractice awards beyond the actual damages suffered.) A number of states have enacted legislation in an attempt to limit such duplication of payments.

The legislation modifying the collateral source rule has taken two different approaches. One approach is to permit the introduction into evidence of compensation or payments received from collateral sources. This places before the jury the total amounts received by a plaintiff prior to trial with the jury being allowed to give whatever consideration it deems appropriate to such amounts relative to the amount of the award it grants.

A second approach is that rather than permitting any collateral source payment to be admissible as evidence, there will be an offset against any award given by the jury in the amount of any collateral source payments received by the plaintiff. Thus, the jury has no knowledge of any collateral source payments received by the plaintiff, and makes its award independent of such amounts. The amount of any collateral source payments received is then deducted from the jury award in determining the amount of the judgment.

Countersuits. Several state medical societies have undertaken to provide various forms of assistance to physicians who think they have been the victims of frivolous medical malpractice suits. Such assistance has included in some instances the preparation of a countersuit.

Countersuits may be based on any one of a number of different legal theories, including either a statutory or common law action for malicious prosecution, abuse of process, or defamation. Such actions, as a rule, may only be brought after the completion of a malpractice action, and then only on a verdict of nonliability.

Excess recovery funds/patient compensation fund. An excess recovery fund is a government-operated mechanism established to pay that portion of any judgment or settlement against a health care provider that is in excess of a statutorily designated amount (eg, $100,000 per occurrence, and $300,000 per year). Thus, while the individual physician's liability is limited, there may or may not be a limit on the overall amount the plaintiff may recover depending on the particular statute in question.

Excess recovery funds are provided through an annual surcharge assessed against health care providers, with such a surcharge often being a specified percentage of the provider's annual insurance premium. The statutes that establish these funds often specify that the amounts received are to be held in trust and invested by the insurance commissioner.

States that have established an excess recovery fund require that participants in the fund either maintain medical malpractice liability insurance in an amount not less than the amount at which the fund becomes operational, or otherwise demonstrate financial responsibility for such an amount. Thus, if the fund is set up to pay judgment amounts in excess of $100,000 per occurrence, then the provider is required to have liability insurance or otherwise demonstrate financial responsibility in an amount equal to $100,000 per occurrence. Failure to maintain such liability insurance or otherwise demonstrate financial responsibility results in the provider not receiving the protection (ie, limited individual liability) of the statute.

Health care mutual insurance companies. A more recent trend to assure the availability of medical malpractice insurance has been legislation authorizing the formation of health care mutual insurance companies, which are often referred to as captive companies. Most often formed by state medical societies, these captive companies are private, physician-owned and operated insurance companies that are authorized to write medical malpractice insurance for the benefit of their members.

The insurance laws of a number of other states already permit the establishment of wholly owned mutual insurance companies, so that additional legislation is unnecessary to authorize creation of physician-owned mutual

companies in those states.

Statutory reserve requirements for captive companies are generally met through an assessment of the physician members, which is normally in the form of a one-time special charge (often in an amount approximately equal to one year's premium), which is payable in addition to the annual premium payment.

Hospital risk management committees. This statute provides for the establishment of an extensive risk management program in all health care facilities, including ambulatory surgical centers, HMOs, hospitals, and nursing homes. Each program is to be administered by a facility-designated "risk manager." Among other requirements, the statute requires that the risk management program provide for "the development and implementation of an incident reporting system based upon the affirmative duty of all health care providers and all agents and employees of the health care facility to report injuries and adverse incidents to the hospital risk manager; and the development and implementation of a program designed to provide compensation to certain persons who are determined to have sustained a compensable injury pursuant to the provision of . . . this Act."

Incident and claim reporting. Several states have enacted legislation requiring that malpractice claims, settlements, or judgments be reported either to the insurance commissioner or to the appropriate licensing board. These statutes most often provide that such reporting be done by insurance carriers. The purpose for such a requirement is to provide information concerning the nature and extent of the medical malpractice problem within a particular state.

Informed consent. The doctrine of informed consent imposes a duty on a health care provider to disclose pertinent information to a patient regarding the nature and purpose of proposed medical treatment and the risks associated with such treatment. The doctrine of informed consent has been formulated through various court decisions. In the past, this practice often resulted in inconsistent applications of the doctrine, and tended to be confusing as to what exactly were the health care provider's disclosure obligations.

Several states have now codified the doctrine of informed consent in an attempt to insure a uniform definition and application of the doctrine. The state statutes generally require that consent to medical treatment be in writing, and impose a duty on a physician to either disclose all facts and circumstances associated with a specific treatment plan, or to disclose only those that may be comprehended by a "reasonable patient."

Itemized verdicts. In most jurisdictions, jury verdict awards for medical malpractice are rendered as a lump-sum award without distinguishing the various elements of the verdict, such as medical expenses, lost income, and general damages (pain and suffering). It is often extremely important to ascertain the amounts awarded for past and future losses; there is no way of doing so unless state law permits itemized verdicts.

Limitation on policy cancellations. A problem that may be encountered by physicians is the sudden cancellation of medical malpractice insurance as a result of an adverse judgment or settlement. Several states have enacted legislation designed to ameliorate this problem. However, many of these statutes do not restrict the circumstances on which cancellation or termination may be exercised, but only require that a written notice of cancellation or termination of a medical malpractice insurance policy be sent at least 30 to 90 days in advance of the termination date.

Limitations on recovery/caps on awards. Several states have enacted legislation that establishes maximum ceilings on the amount of damages that may be recovered in medical malpractice cases. The maximum ceilings discussed herein relate only to the amounts that may be recovered by a plaintiff as opposed to statutory limits placed on the amounts for which an individual provider may be held directly liable, with excess amounts (either limited or unlimited) being recoverable from an excess recovery or patient's compensation fund.

Locality rules. "Locality rules" in medical malpractice cases, which prescribe the standard of care as compared with other similar physicians or health care providers in a designated geographic area, take several forms. For example, a surgeon may be held to a standard of care of a reasonable surgeon within the local community, or within the state, or may be held to a national professional standard. These standards may be applied in a variety of situations. For example, such standards may be applicable both in determining whether there was negligence in regard to care given, and in determining the qualifications of expert witnesses.

- *Expert witness.* Many medical malpractice cases involve extremely difficult and complex medical issues that may only be explained through the use of expert witnesses. Because of the importance expert witnesses play in the outcome of medical malpractice actions, several states have enacted legislation relative to the qualifications and use of expert witnesses.
- *Standard of care.* The standard of care in a medical malpractice action is that level of care to which a health care provider is held accountable to a patient, and is based on the prevailing level of care practiced within a particular locality (community, state, or national). In order to prevail in a malpractice action based upon negligence, the plaintiff must establish the standard of care to which the provider is to be held accountable and must prove that the provider failed to meet such standard.

Mandatory insurance coverage. A number of states have recently enacted legislation requiring that all physicians submit either proof of insurance, sometimes including self-insurance, or proof of financial responsibility within certain specified dollar limitations as a condition of licensure or relicensure within the state.

Notice of intent to sue. Prior to filing a medical malpractice action, an individual has to notify the physician or other health care provider in writing of his intention to sue and of the date of the alleged malpractice. The commencement of an action is then prohibited for a specified number of days (60 to 90 days) after the notice is given.

The theory behind such notice is that it encourages the claimant, physician, and physician's insurance company to investigate the claim and perhaps reach some settlement prior to the initiation of expensive, time-consuming litigation. It is also believed that the parties might be more willing to negotiate a settlement in an informal atmosphere rather than as adversaries in a lawsuit.

For the 60 to 90 days following the giving of notice, the applicable statute date limitation is tolled in order not to

prejudice the plaintiff's cause of action. The statutes also provide a maximum period for bringing suit beyond the statutory time if the notice was sent within 60 or 90 days of the expiration of the limitations period.

Periodic payments. In most states, unless otherwise agreed on by the parties or mandated by the court, judgments may only be rendered as a lump-sum award. This type of payment mechanism is often ill-suited to medical malpractice cases, because awards in such cases often include payment for anticipated future medical care, lost earnings, and pain and suffering. Such awards often require speculation as to such future damages. Furthermore, the premature death of the plaintiff may create a windfall for the plaintiff's heirs where a significant portion of an award is based on such future damages.

Under a periodic payment system, the payments are made over the actual lifetime of the plaintiff or for the actual period of disability. Under this system funds are available for the purpose for which they are intended, and there is no windfall to the beneficiaries of a plaintiff who dies sooner than expected. Also, an insurer can fund periodic payments at substantially less cost than an equivalent lump-sum payment. The savings may be passed on to providers in the form of lower malpractice insurance premiums, or at least in a reduced rate of increase in such premiums, which will mean lower fees for patients.

Premiums. No insurer who provides professional liability insurance for physicians, surgeons, or dentists shall increase the premium for such insurance, impose a surcharge with respect to such insurance, or otherwise require additional compensation for such insurance or institute or increase a deductible amount payable by the insured because a notice of intention to commence an action has been given, unless a complaint has been served on the physician, surgeon, or dentist with respect to such action.

Pre-trial screening panels. Another mechanism designed not necessarily as an alternative but at least as a prerequisite to trial is the pre-trial screening panel. Procedures normally require a mandatory pre-trial hearing to be conducted by a panel comprised of members as dictated by statute. In various combinations, states require that screening panels be composed of physicians, attorneys, and, in some instances, a judicial officer.

Unlike arbitration procedures, pre-trial screening panels are generally conditions precedent to trial and are not in lieu of a court trial. The statutes provide that the plaintiff must file a notice of claim with the pre-trial screening panel prior to filing an action in court.

Under most of the pre-trial screening laws, once a claim has been filed with the panel, a review board is selected to hear evidence on the claim. Normally, the hearing conducted by the panel is informal, and the strict rules of evidence are not applicable.

Pre-trial panels have come under constitutional attack in several states, generally on the theory that such panels infringe on the state's constitutional guarantee of free and open access to state courts.

Punitive damages provisions. Punitive damages are those over and above actual damages suffered by a plaintiff, and are intended solely as a penalty against the defendant. Such damages are generally awarded only in cases where the defendant has acted with malice or with willful and wanton misconduct.

Since medical malpractice cases usually involve only negligence, it would be unusual that punitive damages would be awarded in a medical malpractice case. However, several states have enacted provisions that anticipate the possibility of a punitive damage award in medical malpractice cases.

Reinsurance exchange, professional liability. While the particulars of the exchanges vary from state to state, it is basically an organization comprised of all insurance carriers writing a certain class of insurance within the state. It is established to provide reinsurance for medical malpractice policies written by member companies that may be ceded to the exchange. Profits and losses incurred by the exchange generally are apportioned to the member companies on the basis of premium volume.

The concept of a reinsurance exchange differs from that of a joint underwriting association in several respects. The primary difference between the two concepts is that in a reinsurance exchange program, the responsibility for underwriting and servicing the primary policy is with the carrier writing the policy, whereas in a joint underwriting association program the joint underwriting association has that responsibility.

Remittitur and additur provision. With any malpractice action where damages are awarded to the plaintiff, it is the responsibility of the court, on proper motion, "to review the amount of such award to determine if such amount is clearly excessive or inadequate, it shall order a remittitur or additur as the case may be. If the party adversely affected by such remittitur or additur does not agree, the court shall order a new trial concerning the issue of damages only."

Res ipsa loquitur. This common law doctrine applies when a plaintiff can demonstrate that the injury occurred while the instrumentality causing the injury was under the exclusive control of the defendant and that if used properly, would not, in the mind of the reasonable man, normally cause injury. Under the doctrine, as it was originally applied, the demonstration of these factors created an inference of negligence that, if not rebutted by the defendant, was a sufficient basis for liability. Also, the jury would be permitted but not compelled to accept the inference of negligence in reaching its determination on whether or not the defendant was negligent.

In more recent years, courts in a number of states have expanded the applicability of the doctrine of *res ipsa loquitur*, and have also increased the effect of its applicability from that of a mere inference to that of a presumption, which, if not rebutted, will allow the jury to reach no other finding than guilty.

Respondent in discovery. One problem present in almost all medical malpractice lawsuits is determining the proper party defendant(s), since it is often difficult to determine at what point the alleged malpractice occurred and by whom. In the typical hospital setting, a patient will most likely be seen by a number of physicians, nurses, and other hospital employees.

In preparing to file a lawsuit, the attorney representing the plaintiff often employs a "shotgun" approach by naming as defendants various persons and entities who have

come in contact with the plaintiff during the period in which the alleged malpractice occurred. Many times named defendants are quickly dropped from the lawsuit once the plaintiff realizes through discovery procedures that certain named defendants had no connection with the alleged malpractice.

Statute of frauds (agreements assuring results). Statutes of frauds are rules of law that require certain transactions and agreements to be in writing and signed by the person to be held liable in order to be enforceable in a court of law. The purpose of such statutes is to insure that proof of the transaction is available, thereby lessening the possibility of one party committing a fraud on the other party by pleading a nebulous or nonexistent agreement.

Frequently, misunderstandings occur when a physician offers oral reassurances to a patient, which the patient may interpret as a guarantee of results. Such misinterpretations of oral reassurances may be the basis for a medical malpractice action when the expected results do not occur or when there are complications.

Statute of limitations. A statute of limitations is a law cutting off a cause of action, including medical malpractice actions, after the expiration of a specified time period. With respect to medical malpractice, the statute can begin to run from either the date of occurrence or the date the alleged malpractice was or should have been discovered.

The primary purpose of a statute of limitations is to require that a claim be asserted within a specified time period while the pertinent evidence is available. Also, it is generally believed that the spectre of a lawsuit should not continue for an indefinite time. In the medical malpractice area, a shorter, more definite statute of limitations eliminates a "long tail" in malpractice claims, thereby making the writing of medical malpractice insurance more actuarially predictable.

• *Specific medical malpractice statutes of limitations.* Every state has a statute of limitations applicable to medical malpractice actions. However, in some states the statute is a general one, applicable in all tort actions.

• *Discovery.* A discovery clause pertains to that portion of a limitations statute dealing with the discovery of medical negligence (eg, a foreign object left in the body during surgery) sometime after the actual event took place. The discovery clause places a time limit tolling from the time of discovery to initiate a malpractice action. The discovery clause generally applies to majors and minors equally.

• *Maximum statute of limitations period.* In many states the statute of limitations for malpractice actions begins to run only on discovery of the injury. Since injuries caused by malpractice may be discovered several years after the treatment was rendered, the time period for filing an action may be uncertain. This period of uncertainty is often referred to as the "long tail," and is often cited by insurance companies as a major difficulty in establishing medical malpractice insurance premiums on an actuarially sound basis.

Some states have sought to eliminate the "tail" by placing an absolute maximum time period within which medical malpractice suits may be brought. Such statutes commonly provide for bringing action within a certain number of years after the occurrence of the alleged malpractice and within an additional couple of years (beyond the regular limitation period) where the injury could not have been discovered through the reasonable diligence of the injured person. An exception to the time period is provided in some of these statutes where foreign objects are left in the body, or where the health care provider has fraudulently concealed the fact of injury.

• *Minors.* In most states, statutes of limitations provide that if an injury is incurred by a minor, the statute is tolled (ie, stops running) on the minor's cause of action until he reaches the age of majority.

Several states have amended their statutes of limitations in cases where minors are involved, typically by providing that the statute applies to a minor prior to reaching the age of majority. For example, where a two-year statute of limitations is provided, a state may provide that actions occurring before the age of six years must be brought before the minor's eighth birthday. In statutes of this type, after the minor reaches the age of six the general two-year time limitation becomes applicable for minors as well as for adults. Most of the state statutes that have been modified relative to minors are of this variety.

Type of policy. There are presently two types of insurance policies available for medical malpractice coverage: the claims-made and the occurrence policy. Claims-made policies cover claims reported during the policy period that arise from incidents occurring on or after the inception date of the physician's policy. A physician must therefore purchase additional coverage for a time when he is not practicing medicine, such as retirement, to insure coverage for claims resulting from incidents that occurred during the time the claims-made policy was in effect, but that were filed after the policy dates.

Claims-made rates generally start off lower than occurrence rates and grow progressively higher for the first several years of a physician's coverage. However, the rates level off at the "mature" year.

Occurrence policies cover the physician for claims made and filed from incidents arising during the policy period, and for claims made from incidents arising during the policy but filed after that period. Therefore, under an occurrence policy, a physician would be covered during retirement for claims made involving an incident that occurred during the time he practiced medicine.

MEDICAL MALPRACTICE LEGISLATION IN THE UNITED STATES: 1971–1985	*Ad Damnum*	*Advanced Payments*	*Arbitration*	*Attorney Fee Regulation: Percentage*	*Attorney Fee Regulation: Contingency Fee and Sliding Scale*	*Attorney Fee Regulation: Reasonable Fee*	*Awarding Costs, Expenses, and Fees*	*Burden of Proof*	*Caps on Physicians' Personal Assets*	*Certificate of Meritorious Claim*	*Collateral Sources: Discretionary*	*Collateral Sources: Mandatory Offset*	*Countersuits*	*Informed Consent*	*Itemized Verdicts*	*Limitations on Recovery, Caps on Awards*	*Locality Rules: Expert Witness*	*Locality Rules: Standard of Care*	*Notice of Intent to Sue*
ALABAMA	XR	X	X															X*	X
ALASKA	X	X	X					X				X		X				X	X
ARIZONA	X					XR		X			X*							X	
ARKANSAS	XR						X	X						X	X		X	X	X
CALIFORNIA	X		X		X*					X	X*					X6*			X
COLORADO	X					X	X							XR					
CONNECTICUT	X	X																	
DELAWARE		X			X			X			X			X			X	X	X
FLORIDA	X				X		X							X	X		X	X	X
GEORGIA	XR		X																
HAWAII	X	X			XR	XR								X					
IDAHO				X		XS		X				XR		X		XS	X*	X*	
ILLINOIS	X	X					X									XR			
INDIANA	X*	X		X*	X				X							X*	X		
IOWA	X				X	X						X*		X					
KANSAS	X						X		X5		X*					X7			X
KENTUCKY	X	X												X		XR			
LOUISIANA	X*		X					X						X		X	X	X	
MAINE	X		XR											X					
MARYLAND	X	X	X		X														X
MASSACHUSETTS	X						X*												
MICHIGAN			X*	X															
MINNESOTA																			
MISSISSIPPI	X																		
MISSOURI	X																		
MONTANA																			
NEBRASKA	X	X			X*		X				X*			X		X8*		X	
NEVADA		X						X						X				X	
NEW HAMPSHIRE	XR				XR		XR	XR			XR	XR		XR	XR	XR	XR	XR	XR
NEW JERSEY	X5				X5														

Periodic Payments T	Pre-Trial Screening: Admissible T	Pre-Trial Screening: Nonadmissible T	Punitive Damages T	Remittitur and Additur Provision T	Res Ipsa Loquitur T	Statute of Frauds T	Statute of Limitations: Specific Medical Malpractice T	Statute of Limitations: Discovery T	Statute of Limitations: Maximum Period T	Statute of Limitations: Minors T	Channeling I	Excess Recovery Funds Patient Compensation Fund I	Health Care Mutual Insurance Companies I	Hospital Risk Management Committee I	Incident and Claim Reporting I	Limitation on Cancellation of Policy I	Mandatory Insurance Coverage I	Premiums I	Reinsurance Exchange I	Respondent in Discovery I	Type of Policy: Claims Made I	Type of Policy: Occurrence I
							X*	XR	X*	X*					X						X	X
X	X				X	X	X	X		X			X		X		X				X	X
	X*					X	XR	X		XR			X		X						X	X
X		X					X	X	X	X					X	X			X		X	X
X*					X		X	X	X	X					X			X			X	X
							X*	X*	X*	X		X4			X	X	X					X
	X2						X*		X*							X					X	
X	X		X		X	X	X	X		X					X						X	
X	XR			X	X		X		X			X	X	X							X	X
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	X*						X	X	X	X		X			X	X					X	X
X		X					X	X*	X	X			X	X		X					X	
	X						X	X	X	X			X		X						X	X
		X						X		X											X	X
							X	X		X			X		X							X
							X		X	X					X						X	
							X	X		X			X								X	
		XR					X	X	X	X			X		X						X	X
		X*					X						X		X						X	
	X*					X	X		X			X			X	X	X				X	X
	XR				X		X	X	X	X					XR	X						X
XR		X			XR		X	X	X	XR					XR							X
							XR	X5		XR				X5					X		X	X

MEDICAL MALPRACTICE LEGISLATION IN THE UNITED STATES: 1971–1985	*Ad Damnum* T	*Advanced Payments* T	*Arbitration* T	*Attorney Fee Regulation: Percentage* T	*Attorney Fee Regulation: Contingency Fee and Sliding Scale* T	*Attorney Fee Regulation: Reasonable Fee* T	*Awarding Costs, Expenses, and Fees* T	*Burden of Proof* T	*Caps on Physicians' Personal Assets* T	*Certificate of Meritorious Claim* T	*Collateral Sources: Discretionary* T	*Collateral Sources: Mandatory Offset* T	*Countersuits* T	*Informed Consent* T	*Itemized Verdicts* T	*Limitations on Recovery, Caps on Awards* T	*Locality Rules: Expert Witness* T	*Locality Rules: Standard of Care* T	*Notice of Intent to Sue* T
NEW MEXICO	X	X							X							X9			X
NEW YORK	X			X	X		X				XR	X		X	X				
NORTH CAROLINA	X	X						X						X				X	
NORTH DAKOTA			XR				X	X		X		X		XR		XR	XR	XR	XI
OHIO	X		X									X		X		X6	X*		
OKLAHOMA				X				X									X		
OREGON				X										X				X	
PENNSYLVANIA		X			XR		XR		X5				XR	X					
RHODE ISLAND	X				X		XR				X			X					
SOUTH CAROLINA									X5								XR	XR	
SOUTH DAKOTA			X								X					X			
TENNESSEE	X				X			X				X	X	X			X	X	
TEXAS	X	X						X	X5				X	X		X			
UTAH	X		X	X			X					X		X					X
VERMONT			X					X						X				X	
VIRGINIA			X					X								X	X	X	
WASHINGTON	X	X				X		X			X		X	X				X*	X
WEST VIRGINIA		X						X											
WISCONSIN	X	X				X	X	X	X5						X				X
WYOMING	XR	X				X					X								
KEY TOTAL	29	19	12	7	10	6	11	17	2	2	9	7	3	23	4	11	10	16	12

X—*Legislation enacted.*
XR—*Repealed and or declared unconstitutional by State Supreme Court.*
*—*Challenged and declared constitutional.*
S—*Sunset provision allows expiration.*

TOTAL—*Number of states currently having that particular legislation.*

2—*Admissable only if panel decision is unanimous.*
3—*Only formal panel decisions are admissable.*
4—*Provision enacted but fund never established.*
5—*Via a fund or rule but not by statute.*
6—*Caps on pain and suffering (noneconomic damages).*
7—*Caps on punitive damages only.*
8—*Caps on awards covered by participating voluntary fund.*
9—*Excluding punitive damages.*
10—*Structured awards are not consistently recognized by the courts.*

Periodic Payments ..... T	Pre-Trial Screening: Admissible ..... T	Pre-Trial Screening: Nonadmissible ..... T	Punitive Damages ..... T	Remittitur and Additur Provision ..... T	Res Ipsa Loquitur ..... T	Statute of Frauds ..... T	Statute of Limitations: Specific Medical Malpractice ..... T	Statute of Limitations: Discovery ..... T	Statute of Limitations: Maximum Period ..... T	Statute of Limitations: Minors ..... T	Channeling I	Excess Recovery Funds Patient Compensation Fund I	Health Care Mutual Insurance Companies I	Hospital Risk Management Committee ... I	Incident and Claim Reporting I	Limitation on Cancellation of Policy I	Mandatory Insurance Coverage I	Premiums I	Reinsurance Exchange I	Respondent in Discovery I	Type of Policy: Claims Made I	Type of Policy: Occurrence I
		X					X		X	X		X			X	X					X	X
X	X2						X	X	X	X			X		X						X	X
						X	X	X	X	X		X			X		X		XR		X	
XR	XR				XR		X	X	X	X		X	X		X		XR				X	X
	X*					X	X	X*	X	XR	X										X	X
					X		X*								X							X
			X				X	X	X	X		X			X						X	X
	XR		X			X		X				X				X	X				X	X
	XR				X		X	X	X	XR					X		X					X
X							X	X	X	X		X	X		X							
							X	X	X	X			X		X						X	X
	XS				X		X*	X	X*				X		X							X
					X	X	X	X	X	X			X			X					X	X
		X				X	X*	X	X						X						X	X
						X	X														X	
	X						X		X	X											X	X
					X		X	X	X				X								X	
																					X	X
X*	X3*					X	X	X	X	X	X	X			X	X					X	X
X10						X	X		X		X	X4			X						X	X
11	13	10	3	1	11	14	45	34	36	32	3	15	18	2	34	12	8	1	2	1	42	37

TABLE I. Medical Malpractice Legislation Enacted in the United States: 1971–1985

State	Have provisions for:	Do not have provisions for:
Alabama	Claims made and occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
Alaska	Claims made and occurrence policies Collateral sources Periodic payments (of which the jury cannot be advised)	Caps on awards Caps on physicians' personal assets Contingency fees
Highest premium for $5 million/$5 million is $40,246 annually.		
Arizona	Claims made and occurrence policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees Periodic payments
Highest premium for $3 million coverage is $30,000 annually. $5 million/$5 million coverage is also available.		
Arkansas	Claims made and occurrence policies Collateral sources Periodic payments	Caps on awards Caps on physicians' personal assets Contingency fees
Average premiums range between $900 and $7,000 annually. $7,000 is the highest in the state.		
California	Claims made and occurrence policies Caps on awards Collateral sources Contingency fees Periodic payments	Caps on physicians' personal assets
The highest premium for $1 million/$3 million coverage is $51,920 annually for neurosurgeons. $10 million/$10 million is also available. $2 million/$4 million is the most common, but there are a large number of $5 million/$5 million policies. A cap on pain and suffering (noneconomic damages) has been in effect since 1975 ($250,000) and was upheld by the Supreme Court this year. As far as an effect on premium costs, it will have more of an impact now and in the next few years than it had previously. However, there are already signs that trial lawyers will go for higher economic damages. Proposals have been made to this effect, and also to raise the level of the cap.		
Colorado	Occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
Average premiums range from $1,600 to $26,000 annually.		
Connecticut	Claims made policies Collateral sources	Caps on awards Caps on physicians' personal assets
Contingency fees and periodic payments are not mandated but are used, the latter in large settlements. The highest premium for neurosurgeons, cardiologists, and orthopedic specialists is $27,000 annually, but will rise to $31,800 after an 18% increase. The highest coverage available is $1 million.		
Delaware	Claims made policies Collateral sources Contingency fees (the fee schedule is 35% on first $100,000; 25% on next $100,000; and 10% on the balance) Periodic payments	Caps on awards Caps on physicians' personal assets
Average premiums range between $5,000 and $10,000 annually. The highest premium is $21,000 for fourth year obstetrician/gynecologists.		
Florida	Claims made and occurrence policies Contingency fees (the fee scale is subject to Supreme Court changes; the sliding scale ranges from 15% to 45% depending on the point at which the case is settled, with 15% on awards in excess of $2 million) Periodic payments (on awards greater than $500,000)	Caps on awards Caps on physicians' personal assets Collateral sources
The highest premium (for obstetric surgeons and neurosurgeons) is $78,450 ($100,000/$300,000). The highest coverage is $1 million/$3 million.		
Georgia	Claims made policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The highest premium is $37,000 annually. The highest coverage is $10 million/$10 million.		

Hawaii	Claims made policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees (attorney fees must be approved by the court) Periodic payments
The highest premiums are $33,000 annually. Total physician liability is $5 million/$5 million.		
Idaho	Claims made and occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
Caps, collateral sources, and contingency fees had statutes but were declared unconstitutional several years ago.		
Illinois	Claims made and occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The highest premium is $83,000 for neurosurgeons and total physician liability is $5 million/$5 million. Most physicians carry $1 million/$3 million.		
Indiana	Claims made and occurrence policies (4 companies writing occurrence policies; 1 writing claims made policies with a long tail) Caps on awards Caps on physicians' personal assets Contingency fees (via a statute-created patients' compensation fund) Periodic payments	Collateral sources
The $500,000 cap on awards has been considered responsible for keeping premiums low.		
Iowa	Claims made and occurrence policies (although moving towards claims made policies only) Collateral sources Contingency fees	Caps on awards Caps on physicians' personal assets Periodic payments
Modified collateral sources provision and contingency fees are not statutorily mandated, but are used. The highest coverage available is $5 million.		
Kansas	Claims made and occurrence policies Collateral sources	Caps on awards Contingency fees (attorneys' fees are not covered by statute, but are expected to be reasonable, generally 25% to 50% of settlement) Periodic payments
Physicians' personal assets and awards beyond coverage are covered via a "health care stability fund," which adds a 110% surcharge on premiums. Physicians who cannot get coverage through two companies possibly get it through a joint underwriting association if they pass a personal interview that determines the physician's willingness to properly inform patients. There is a cap on punitive damages and the premiums vary.		
Kentucky	Claims made policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
Louisiana	Claims made and occurrence policies Caps on awards Periodic payments (used via authority of the Attorney Generals office)	Caps on physicians' personal assets Collateral sources Contingency fees
Since 1975 there have been three caps of $500,000 each: medical malpractice for private physicians; medical malpractice for employers of physicians in Louisiana; and state liability for all other tort actions. The highest premium is in the range of $21,000 annually.		
Maine	Claims made Periodic payments	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees
Monthly meetings have been instituted with trial lawyers in response to their liability crisis. Highest premium is $40,000 annually for neurosurgeons.		
Maryland	Claims made and occurrence policies Contingency fee (allows judge to review attorney's fees) Periodic payments (optional)	Caps on awards Caps on physicians' personal assets Collateral sources
The highest premium for obstetrician/gynecologists is $35,000 for $1 million/$3 million coverage. The highest coverage is $1 million/$3 million with a $5 million excess.		

Massachusetts	Claims made and occurrence policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees (although there is no statutory provision, they are used: 33⅓% to 50%) Periodic payments
The highest premium is $15,300 for orthopedic specialists, plastic surgeons, neurosurgeons, and obstetrician/gynecologists)		
Michigan	Occurrence policies Contingency fees (court rule allows 33%)	Caps on awards Caps on physicians' personal assets Collateral sources Periodic payments
The highest premium is $55,000 for obstetrician/gynecologists and neurosurgeons. The highest coverage is $1 million/$1 million.		
Minnesota	Claims made policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The highest policy is $20,000 annually and total physician's liability is $4 million/$5 million.		
Mississippi	Modified claims made policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees Periodic payments
Although there are no provisions for contingency fees and periodic payments they are used. The highest premium for neurosurgeons and anesthesiologists is $31,000 annually. The highest coverage available is $5 million/$5 million.		
Missouri	Claims made and occurrence policies (although moving toward claims made policies only)	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments (although not statutorily mandated, the judge may opt for it)
The range of premiums is $1,200 to $34,000. Total physician's liability is $5 million/$5 million.		
Montana	Claims made policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The highest premium is $20,000 annually.		
Nebraska	Claims made and occurrence policies Caps on awards (covered via a participating voluntary state fund with a cap of $1 million) Collateral sources Contingency fees	Caps on physicians' personal assets Periodic payments
The highest premium is about $11,000 annually and total physician liability is $1 million/$3 million.		
Nevada	Occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
Although there are no provisions for contingency fees, they are used; generally 30% to 40% but can go up to 50%. The highest premium is $44,160 for $1 million/$3 million coverage. The highest coverage available is $5 million/$7 million.		
New Hampshire	Occurrence policies (although moving toward claims made policies)	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
New Jersey	Claims made and occurrence policies Contingency fees (sliding scale)	Caps on awards Caps on physicians' personal assets Collateral sources Periodic payments
The average premium is $9,000; the highest is $30,000 for neurosurgeons with $1 million/$1 million coverage. The highest coverage available is $5 million. Currently before legislature is a four part bill that includes caps on awards, collateral sources, periodic payments, expert witness, and certificate of meritorious claim.		

New Mexico	Claims made policies Caps on awards (excluding punitive damages) Caps on physicians' personal assets	Collateral sources Contingency fees Periodic payments

Since 1976 have had a $500,000 cap on awards excluding punitive damages and this may have had an effect on premium costs. The courts are conservative; only two cases have been awarded $500,000. The conservative climate, the cap, and the malpractice bill are the measures that keep the premiums low.

New York	Claims made and occurrence policies Collateral sources Contingency fees (33⅓–30% of first $250,000; 25% next $250,000; 20% next $500,000; 15% next $250,000; and 10% of any further amount) Periodic payments	Caps on awards Caps on physicians' personal assets

The highest premium is $83,000 for neurosurgeons, with coverage of $1 million/$3 million.
New York physicians pay the highest premium rates overall in the country.

North Carolina	Claims made policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees Periodic payments

Although contingency fees are not a statutory provision, they are used; the average is 20% to 30%.
The highest premium is $17,000 for neurosurgeons. $5 million/$5 million coverage is available.

North Dakota	Claims made and occurrence policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees

Although contingency fees are not a statutory provision, they are used; generally 33⅓%.
The average premium is variable and the highest is $45,000 for neurosurgeons. The highest coverage available is $10 million.

Ohio	Claims made and occurrence policies Collateral sources	Caps on awards Caps on physicians' personal assets Contingency fees Periodic payments

Current bills will attempt for a cap on punitive damage and certain economic damages, contingency fees, and periodic payments.
It is felt that the situation is deteriorating rapidly. Major hospital carriers are requiring medical staffs to change bylaws to include as criteria for membership that a physician carry $1 million coverage. However, it is felt that this will only encourage larger awards.
The highest premium is $17,000 for neurosurgeons with coverage of $1 million/$3 million. The highest coverage is $5 million. There is a $250,000 cap on pain and suffering and collateral sources provision.
The state has had a $250,000 cap since 1975 on noneconomic damages; there is no cap on economic or punitive damages.

Oklahoma	Occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments

Neither contingency fees or periodic payments are statutorily mandated but may be used (contingency fees are generally 40 to 50% of award).
The average premium is $4,000 and the highest premium is $12,000 for obstetrician/gynecologists, neurosurgeons, and plastic surgeons with a coverage of $1 million/$3 million.

Oregon	Claims made and occurrence policies Contingency fees (35% on first $100,000; 35% on next $100,000; and 10% on balance)	Caps on awards Caps on physicians' personal assets Collateral sources Periodic payments

The highest premium for $5 million coverage is $40,000 annually, and is going to $64,000 in 1986 for neurosurgeons.

Pennsylvania	Claims made and occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments

No limit to amount of insurance a physician may buy. A catastrophic loss fund covers $1 million, including personal assets.

Rhode Island	Occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments

Periodic payments not statutorily mandated; in actuality they are used.
The highest premium is $30,000 for $1 million/$3 million coverage.

South Carolina	Periodic payments Caps on physicians' personal assets (covered through a patients' compensation fund with no cap).	Caps on awards Collateral sources Contingency fees
The highest premium for coverage of $1 million/$3 million is $5,600 for a neurosurgeon.		
South Dakota	Claims made and occurrence policies Caps on awards Collateral sources Contingency fees	Caps on physicians' personal assets Periodic payments
The state has had a $500,000 cap on general damages since 1974; however, premium rates continue to increase. The highest premium is $32,000 annually for orthopedic surgeons and neurosurgeons. Physicians may buy as high a policy as they wish.		
Tennessee	Occurrence policies Collateral sources Contingency fees (maximum of 33%)	Caps on awards Caps on physicians' personal assets Periodic payments
There is no provision for periodic payments but the judge may use such a method. The highest premium is approximately $30,000 annually.		
Texas	Claims made and occurrence policies (although moving toward claims made policies) Caps on awards Caps on physicians' personal assets (the Homestead rule covers physicians' personal assets) Collateral sources	Contingency fees Periodic payments
Contingency fees and periodic payments are not statutorily mandated, but are used. There has been a $500,000 cap on awards since 1975. This cap is now being challenged. It has been felt that the cap has had a positive effect on keeping premium costs down. The highest coverage is $1 million/$3 million.		
Utah	Occurrence policies (although moving toward claims made policies) Collateral sources Contingency fees (33⅓%)	Caps on awards Caps on physicians' personal assets Periodic payments
The highest policy available is $18,600 annually.		
Vermont	Claims made	Caps on awards Caps on physicians's personal assets Collateral sources Contingency fees Periodic payments
Contingency fees not mandated but used. Rural community and general conservative climate keep situation under control. The highest premium for $1 million/$3 million coverage for neurosurgeons is $10,889 or $24,622, depending on the company (mature rates). The highest coverage is $1 million/$3 million with a $9 million excess.		
Virginia	Claims made and occurrence policies Caps on awards ($1 million) Contingency fees	Caps on physicians' personal assets Collateral sources Periodic payments
The highest premium is $42,000 annually for neurosurgeons. The highest coverage is $5 million.		
Washington	Claims made policies (initiated in 1986)	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The average premium is $8,500 and the highest premium is $25,690 with coverage of $1 million for neurosurgeons. The highest coverage available is $5 million/$7 million.		
West Virginia	Claims made and occurrence policies	Caps on awards Caps on physicians' personal assets Collateral sources Contingency fees Periodic payments
The average premium is $11,700 and the highest is $48,000 for neurosurgeons. There is coverage of $10 million available.		
Wisconsin	Claims made and occurrence policies (85 to 90% are the latter) Caps on physicians' personal assets Periodic payments (used for awards of future damages of $1 million)	Caps on awards Collateral sources Contingency fees
A physician is required to purchase $200,000 coverage, which makes him eligible for a patients' compensation fund. Awards beyond his coverage and personal assets are handled via this fund. Contingency fees are not statutorily mandated, but are used. The highest premium is $44,600 annually for neurosurgeons.		

Wyoming	Claims made and occurrence policies	Caps on awards
	Collateral sources	Caps on physicians' personal assets
	Structured awards (not consistently recognized by the courts)	Contingency fees

The highest premium for $1 million coverage is under $20,000 annually.

1987 Albert H. Douglas Memorial Award for excellence in clinical teaching

The Medical Society of the State of New York is accepting nominations for the 1987 Albert H. Douglas Memorial Award until October 1, 1986.

> The Douglas Award, consisting of a $500 stipend and a scroll, was established eight years ago to honor an outstanding clinical teacher in all branches of medicine. It is named for the late Dr Douglas, who was a pioneer cardiologist and professor of clinical medicine at the State University of New York Stony Brook Medical Center.

Nominators must complete and submit the official nomination form with additional support information which must include the nominee's curriculum vitae and a personal letter(s) supporting the nomination.

Nominations are invited from undergraduate and graduate medical students and faculty. Please submit the material by October 1, 1986 to:

Scientific Program Committee
Medical Society of the State of New York
420 Lakeville Road, Lake Success, New York 11042

The impact of the malpractice insurance crisis on family physicians in New York State

LINDA ROBINSON, MD

The malpractice insurance crisis in New York State has affected all specialties of medicine. For the most part, surgical subspecialists have received most of the media attention, for in dollar terms their premiums have been the highest. However, family physicians, particularly those in inner city and rural locations, are facing their own unique crisis.

"Family practice is comprehensive medical care with particular emphasis on the family unit, in which the physician's continuing, comprehensive responsibility for health care is not limited by the patient's age or sex nor a particular organ system or disease entity."[1] The family physician is trained to provide health maintenance to patients and to serve as an advocate in health related matters, appropriately utilizing consultants and community resources.

The medical malpractice situation affects family physicians in special ways owing to the nature of the primary care relationship and the style of medicine practiced. The past, present, and future status of the specialty may be at risk if the liability problem is not satisfactorily resolved. Escalating malpractice claims and the cost of their defense serve to undermine well-earned trust, jeopardize access to care, and may threaten the future growth of family practice in New York State.

PAST TRUST IS LOST

The family physician traditionally has been the trusted medical caregiver to the family. Decades ago, the general practitioner, before the age of specialization and subspecialization, usually treated most Americans for almost all illnesses. The image of Marcus Welby, even after 20 years, still lingers with the public as a positive image of a physician. Because of the trust established by close and continuous care, often involving three generations of a family, it was rare indeed for a family physician to be sued. However, this has changed. A survey by the American Academy of Family Physicians in 1984 found that more than one in five of its active members had been involved in a malpractice suit in the previous five years.[2]

The common reactions of physicians to lawsuits are anxiety, anger, and depression.[3] Because of the long-term relationship usually shared by a physician with a patient in family practice, a lawsuit can be particularly devastating. The loss of trust is not only that of a doctor in his patient, but also of a patient in his doctor. The physician fears that any and every patient may sue; patients, through the publicity of litigation, fear their physician may harm them. The trust that is a necessary component to the art of healing is thus lost.

LIMITING ACCESS TO CARE

With rising malpractice premiums, family physicians are faced with difficult decisions. A typical practice has overhead costs of approximately 50% of gross revenues. When large increases in malpractice premiums are announced, a physician may meet the increased expense by raising fees. However, increasing fees may represent a moral dilemma by excluding certain patients from medical care. Rural and inner-city areas are populated by patients who cannot afford to have higher fees passed on to them. When patients cannot pay those fees, they may forego medical care. "Economic factors are a barrier to health care for many rural Americans. Rural Americans are more likely to be elderly, poor, and unemployed than their urban counterparts."[4] In such areas, family physicians treat a high percentage of Medicaid patients. Their Medicare reimbursement is fixed and is lower than that paid for equivalent work in urban areas. Out of economic necessity, some family physicians have reluctantly begun to accept no new Medicaid patients into their practices.

At the present time, 75% of all physicians provide some either free or reduced-fee care, reducing their incomes by approximately 9%.[5] In New York State, family physicians are caring for significant numbers of the poor; it is reported that in the northern part of New York State some family physicians in private practice have up to 50% Medicaid patients under their care.

A preliminary study of the outcome of increasing malpractice fees was undertaken by survey. The results are shown in the Table.

"For almost 20 years the United States has demonstrated a strong commitment to the value that access to care should be available to all and should not be rationed by income, race or region."[6] Malpractice premiums have an insidious way of rationing care.

Other options available for family physicians in New York State who are faced with premiums that their patients cannot afford are to restrict their medical practice, stop providing obstetrical care, stop performing minor office surgery, and stop assisting in surgical procedures. However, these limit the scope of the family physician. Some physicians reduce their practice to part-time, thereby decreasing their premiums by one half. Others prefer early retirement or relocation of their practice to another

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TABLE. Results of a Poll of 115 Active Members of the New York State Academy of Family Physicians April-May 1986*

Fees	Number
Raised fees due to malpractice premiums	84 (73%)
Reduced or discontinued accepting new Medicaid patients	47 (41%)
Reduced charity care	24 (21%)
Ordered more diagnostic tests	54 (47%)
Increased use of consultants	60 (52%)

* Based on a survey conducted by the membership committee of the New York State Academy of Family Physicians.

state. Unfortunately, there is a bimodal curve to the age distribution of family physicians. Even before the malpractice problem, family physicians were in short supply. Nationally, "of the 25,600 general practitioners still active in 1985, well over half were aged 55 or over, and few will be in practice 10 years from now."[7] In rural areas "there are now two main cohorts of primary care physicians: a dwindling number of older general practitioners and a slowly growing number of younger family physicians. As older general practitioners die and retire, many rural areas will be unable to attract physicians to take their place."[4] New York State is often cited as having a "surplus of physicians." There are, however, 75 federally designated health manpower shortage areas in New York State.[8] In addition, there are 224 state designated primary care physician shortage areas where there are an identified 4 million underserved New York State residents.[9]

The malpractice crisis has affected the style of practice of many family physicians. Most physicians surveyed reported practicing defensive medicine. During family practice training, residency programs have traditionally not only taught the use of diagnostic tests but the cost and the appropriate time sequences in which to order them. After graduation, the wisdom of this approach is sidestepped by exhaustive panels of tests in order to avoid litigation. This method of ruling out disease is akin to killing a mosquito with an elephant gun.

Most family physicians pride themselves in being able to treat 90% of the illnesses with which patients routinely present themselves to the office. Due to rising malpractice claims, family physicians are more likely to refer to other specialists now as noted by AAFP Board Chairman Robert D. McGinnis.

The Future Threat

For the past ten years the number of family physicians practicing in New York State has been declining. Nationally, the perceived need for family physicians is such that Congress appropriated $36 million in 1985 to family practice residency programs and $7 million to medical school departments of family medicine.[10] In New York State, aid to family practice residency programs amounts to $3.5 million. One half of all family practice residents after graduation settle in population areas of 25,000 or less.[11] A survey conducted in 1980 demonstrated that of the 170 New York State family practice residency graduates who responded, most came from low population density areas and reported setting up their practices in similar low population areas.[12] These are among the many areas in New York State that presently need family physicians.

New York graduates 100 residents each year from its 20 residency programs in family practice. After graduation, each resident must decide the best location in which to set up a practice. Many medical students are more than $30,000 in debt on graduating from medical school.[13] The opening of a private practice requires going into significant further debt. To this is added the burden of the malpractice premium. The cost of malpractice insurance in rural New York is higher than in some cities in other states. Rates may climb by 50% per year and, in addition, retroactive increases may be assessed. This has sent some young physicians back to the bank for additional loans.

As of April 1986, family practice residencies were contacted by the author in order to learn how many graduates would be leaving New York State after June 1986. Of the current number of graduates (100), 33 plan to move out of state either due to public health or military commitments, because they are returning to their home state, or because they are taking positions elsewhere. Many were still undecided. Over the past year, the New York State Academy of Family Physicians lost 26 members by death. Nonmember physicians could not be accounted for, and those who retired or changed their practice to part-time remain uncounted. A permanent resolution to the medical liability problem might entice more residents to practice in New York State, and to keep those physicians already in practice away from early retirement.

Marcus Welby, MD, hopes for a solution to this malpractice problem. He would like to regain the trust of his patients, to accept all those in need of medical treatment without financial discrimination, and find a young physician to join him in practice.

Acknowledgment. The author wishes to thank Dr Henry Dobies, president of the New York Academy of Family Physicians, for his kind permission in releasing preliminary membership malpractice data.

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A proposed solution to the malpractice problem

VICTOR HERBERT, MD, JD

As a physician and attorney, I was disappointed that the Andrew Stein article (*New York Times*, February 2, 1986) on "Doctors who get away with maiming and killing" and the article on the lawyers-vs-doctors battle on malpractice (*New York Times*, February 14, 1986, p 16) did not delineate the logical three-pronged solution to the malpractice problem: adequate mandatory reporting of incompetence, a streamlined license revocation system, and no-fault legislation.

In a no-fault system, the two issues of injury and fault are separately tried. There is a determination as to whether the patient was injured (ie, a workmen's compensation-type hearing). This determination does not rely on whether or not the physician practiced competent medicine. If the patient was injured, there is appropriate medical and financial redress for the injury.

There is also a separate determination as to whether the physician performed competently. If yes, that is the end of the matter. However, if not, a determination is then made as to whether this was an error by a usually competent physician, or if the physician has a pattern of incompetent performance. If it is an error by a usually competent physician, he is placed on probation and scrutinized for an appropriate period. If he has a pattern of incompetent performance, his license is revoked.

The fault system rarely removes incompetent physicians from practice, a point the American Bar Association appears to ignore. Incompetent physicians may lose or settle out of court many malpractice suits and continue in practice. State licensing boards are rarely notified of the suits or the settlements.

Anyone who wishes to file a malpractice suit should be mandated to file a copy of their complaint with the Office of Professional Medical Conduct of the New York State Department of Health. That office should be given the funds, personnel, and authority to expeditiously investigate, conduct misconduct proceedings, and take final disciplinary actions. Individual victimized patients often do not know they have been victimized and do not come forward, so patient records of physicians reasonably suspected of a pattern of incompetence should be discoverable by subpoena. A reasonable suspicion would be that patients are asked to sign an informed consent that says they understand what the physician does is unconventional, but they want it anyway. About $1 billion per year are taken from patients by physicians in New York State who have patients sign such forms.

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THE CURRENT COURSE OF MISCONDUCT ALLEGATIONS

Currently, allegations of misconduct must run a tortuous course: from the Office of Professional Medical Conduct, to the Department of Health for initial investigation, and to the Board of Regents for final disciplinary action. In recent years, I have brought charges of professional misconduct against several egregious offenders engaged in a pattern of fraudulent and incompetent practice. All of them are still being investigated; all of them are also still practicing. The current system is so slow and tortuous that some of them are on "hold" interminably, sometimes because they have gotten a court to bar access to their patient records, allegedly to "protect the patient's privacy" (often without asking the patient if they want their privacy "protected").

I testified about some of these offenders before US Congressman Claude Pepper's hearing on "Quackery: A $10-Billion Scandal" on May 31, 1984,[1] and before the New York State Assembly Republican Task Force on Health Fraud and the Elderly on December 3, 1985.[2] It is no secret that these physicians are all still practicing.

MISCONDUCT REPORTING REQUIREMENTS

For those of my colleagues who may not be fully aware of what they are required to report, let me quote from the September 1984 "Message to Licensed Professionals Practicing in New York State" from the State Education Department, Office of the Professions[3]:

> Professional misconduct includes: practicing fraudulently, negligently, or incompetently; practicing while being impaired by alcohol, drugs, or mental disability; being convicted of a crime, and similar serious matters. Some examples of misconduct are: physically abusing a patient, not keeping proper records, ordering excessive tests, behaving in a way that indicates moral unfitness, providing treatment or services which were not authorized, neglecting a patient in need of immediate care, guaranteeing a cure, and others.
>
> Fee disagreements do not represent misconduct; however, double billing or other fraudulent billing or charges for unnecessary services, tests or procedures does constitute misconduct.
>
> Telephone calls or letters reporting professional misconduct will be treated confidentially. To report misconduct, for health

professions other than medicine one should write to the New York State Education Department, Office of Professional Discipline, 622 Third Ave, New York, NY 10017. To report misconduct involving physicians, one should write to or call the Office of Professional Medical Conduct, NYS Department of Health, Empire State Plaza, Tower Building, Albany, NY 12237, Telephone: (518) 474-8357.

New York State physicians are not only required by law[3] to report misconduct, but failure to do so is itself misconduct under New York law.[3]

Advantages of the No-fault Approach

No-fault legislation protects patients by assuring redress for injury regardless of whether or not the physician was at fault. It protects the physician against exorbitant malpractice premiums and harassment lawsuits. It protects the courts against being swamped by protracted adversary proceedings whose beneficiaries are the attorneys for both sides. A landmark 1971 study of medical malpractice by the Center for the Study of Democratic Institutions (Santa Barbara, CA)[4] estimated that only 16% of every malpractice dollar went to patients, with most of the rest going to lawyers and insurance companies.

Under elective no-fault,[5,6] with or without an enabling statute,[7,8] one can contemplate that participating physicians could avoid litigation, generously double the payout to patients, give the insurance companies a reasonable profit, and still halve their insurance premiums. The physician elects to pay for such injuries as he chooses to include in the agreement on a no-fault basis, just as employers may elect to be not at all, partially, or fully covered by workmen's compensation, thereby avoiding regular tort liability. Elective no-fault liability may be arranged by contract with the health-care provider himself, without or with the aid of an insurer, and without or with an enabling statute. The physician would select all, or if he chooses just certain risks of personal injury, and agree to pay only for out-of-pocket losses above amounts payable from collateral sources such as Blue Cross, sick leave, and perhaps term life insurance. There would be no payment for pain and suffering, and payment for wage loss could be limited to a maximum of a specific number of dollars per week, with payments made periodically as losses accrued, and not in a lump sum.

In an editorial published more than a decade ago,[9] law professor Jeffrey O'Connell concluded that "malpractice litigation inhibits discovery of malpractice more than uncovering it." In his book, *Ending Insult to Injury: No-Fault Insurance for Products and Services*,[5] he presents a lucid and compelling case for the application of the no-fault concept to medical care, pointing out case after case where the jury decision had nothing to do with whether or not the physician practiced incompetent medicine. In 1986, he made an excellent case for model state no-fault legislation, which he drafted as a bill that Representatives Henson Moore of Louisiana and Richard Gephardt of Missouri have put before the US Congress.[10]

Some very good trial attorneys justifiably think they provide the only redress for injured patients in a system without this triad of adequate mandatory reporting of incompetence, a streamlined license revocation system, and no-fault. It is now time for all states to adopt this triad.

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Preventing medical negligence in caring for infants and children

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The following observations are based on 15 years of experience in reviewing cases of medical malpractice on both a part-time and full-time basis. This experience centered on providing expert opinion as to the defensibility of medical diagnostic judgments. There are several diagnostic problems that are frequently the focus of litigation. It is useful to examine these problems along with the measures that can often prevent subsequent litigation.

MISSED DIAGNOSIS OF HYDROCEPHALUS

A baby's head circumference should be measured at every office visit. If this measurement is simply written down in the office records, it will be of no practical use. On the other hand, if the measurement is charted on a graph, any abnormal trend will be quickly evident. Normal height, weight, and head circumference graphs are readily available and should be routinely used. If the head circumference shows a trend toward the upper limits of normal while the fontanel remains open, a sonogram will easily resolve the dilemma. After the fontanel has closed, a computerized tomographic (CT) scan should be performed.

MISSED DIAGNOSIS OF SCOLIOSIS

This condition is eight times more common in adolescent girls than boys and it is also an easy diagnosis to make. The physician has the patient undress, and facing away from the examiner, bend forward from the waist. In this posture it is easy to see any asymmetry of the back indicating scoliosis. This condition tends to be accentuated by the growth spurt that occurs during puberty. When the diagnosis is made early it may be treated with modern, light-weight plastic braces. For some patients, this bracing will prevent progression of the curve and may avoid the need for surgical intervention. School nurses often perform this simple examination and pass their findings along to the child's doctor. Several files have been reviewed, where the diagnosis was suggested by a seamstress who found one shoulder to be higher than the other while fitting a young lady for her graduation dress.

MISSED DIAGNOSIS OF HYPOTHYROIDISM

Since hypothyroidism is usually not clinically recognizable at birth, New York State, as well as most states, requires a mandatory blood test for inheritable metabolic disease. A blood sample is taken from the baby and processed by the New York State Department of Health Laboratories. The results are sent to the hospital where the child was born. However, any laboratory can make a mistake; thus a word to the wise is sufficient. If the baby's height and weight gain is slow, or if there is constipation or persistent jaundice, one should be wary. Infants with hypothyroidism seldom cry, sleep little, and have poor appetites. At this point, the blood test (metabolic screen) should be repeated. One should be suspicious that all is not well long before flaking dry skin, coarse lusterless hair, lethargy, and enlargement of the tongue make the clinical diagnosis obvious.

MISSED DIAGNOSIS OF CONGENITAL DISLOCATION OF THE HIP

This diagnosis may be suspected in the newborn nursery if flexion and abduction of the hip result in a palpable and sometimes audible click (Ortolani's sign). There may be marked limitation to abduction of the hip. The baby will not kick the affected leg as much as the other in unilateral cases, and the mother may have difficulty diapering on the affected side. As time goes on, asymmetrical skin folds develop in the groin and the affected leg becomes shorter. Early diagnosis permits the use of a harness to abduct the hips and may avoid the need for later surgical correction. If there is any question at all that the hips are not perfectly normal, appropriate orthopedic consultation should be arranged.

FAILURE TO MAINTAIN ADEQUATE PATIENT RECORDS

The most common, overall recurring problem in medical malpractice is widespread lack of documentation with inadequate, sometimes illegible office records and notes in hospital charts. Occasionally one finds in malpractice cases that there are no office records at all. It is difficult, if not impossible, to defend a physician's actions without appropriate documentation.

Examples of this are the following. Children recovering from chicken pox or influenza are at risk of developing Reye's syndrome. An office note stating *GIVE NO ASPIRIN* or an equivalent statement shows that the physician is aware of this possibility. A note of this kind is often the key to a physician's defense in a medical malpractice lawsuit.

Following a head injury, if the neurologic examination

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and skull radiographs are normal, an office note that specifies the parents have been warned to watch for vomiting, lethargy, and other signs is prudent and good medical practice. Some physicians even go to the extreme of having the parents sign a form that they have heard and understood the signs and symptoms to watch for. From a certain perspective this latter action reflects the defensive medicine practiced today.

It may sound oversimplified, but a physician must practice the very best medicine possible and explicitly document all actions taken. If a mistake is made, it should be documented clearly and honestly. Virtually all physicians make a diagnostic or therapeutic mistake at some point in their careers.

In some instances physicians are completely honest and open with the patient, admit to negligence, and then correct the problem. Some patients in these situations conclude that as long as medicine is practiced by human beings it is going to be imperfect, and refuse to bring a lawsuit. Such understanding and such good people do exist.

It is not possible to overemphasize the crucial importance of complete, accurate, and explicit office and hospital progress notes. These are a clear reflection of any physician's style in the daily practice of medicine. Should a physician be named in a malpractice suit, office records and the notes in a patient's hospital chart constitute the basis for a successful defense. Through them a physician's competence, conscientiousness, dedication, and other professional and personal characteristics are often judged.

These suggestions are offered in the hope of being helpful to all physicians who treat and care for children.

Acknowledgment. The author thanks Drs Dennis Allendorf and Tarek Mardam-Bey for their assistance.

NEWS BRIEFS

Maryland caps pain and suffering awards in personal injury cases

Maryland has become the 14th state to approve a cap on awards in personal injury cases, with the passing of liability reform legislation in April. According to the *New York Times*, Maryland's new law, providing a cap of $350,000 on pain and suffering awards in all negligence cases, is the most sweeping reform in the nation. Maryland's cap is the first that extends beyond medical liability suits to suits against all types of businesses and professionals. The cap does not interfere with awards for compensation for lost wages and actual medical costs.

Maryland's reform law also eliminates testimony from so-called "hired guns," expert witnesses who spend more than 20% of their time testifying in negligence cases and are not regarded as objective witnesses. Greater regulatory powers for the state insurance department and changes in insurance law were also part of the reform package.

Physicians attend rally in Albany

About 1,500 physicians braved soaking rains and chill winds to march to the steps of the Capitol building in Albany, calling on the governor and the legislature to produce long-promised medical liability reform.

The march, which followed a rally at the Palace Theatre in Albany, was part of the Medical Society of the State of New York's (MSSNY) second March on Albany for Liability Reform, held on May 21.

A distinguished speakers list attracted about 2,000 physicians, spouses, and other concerned parties to the Palace Theatre to open the day's activities. The physicians were greeted by John A. Finkbeiner, MD, president, and George J. Lawrence, MD, executive vice president of MSSNY, and heard several speakers, including Commissioner of Health David A. Axelrod, MD and Congressman Robert J. Mrazek, D-Long Island.

Emotions ran high at the rally. Angry and frustrated physicians shouted and booed Dr Axelrod during his speech, particularly when he insisted that Governor Mario M. Cuomo would not support a cap on pain and suffering awards, one of the major proposals the physicians seek. He reiterated that the governor was committed to liability reform; the governor suggested several new proposals at a morning meeting with MSSNY officials before the rally, Axelrod said, refusing to elaborate on these proposals.

Congressman Mrazek, author of HR 2659, the Medical Malpractice Reform Act, enjoyed a friendlier reception. The legislation recommends removing malpractice claims from the court system, using instead an arbitration system to determine liability and suggest awards. The bill also calls for tort reforms such as structured settlements, limits on legal fees, and a cap on pain and suffering awards. Allowing an impartial body to determine liability could reduce the possibility of awards prompted by sympathy for an injured plaintiff, Mrazek said. "Arbitration can address the line between negligence and bad results," he stated.

A downpour greeted physicians as they left the Palace Theatre for the march to the Capitol. Some physicians boarded buses, electing to ride rather than walk to the Capitol, but many hardy participants forged into the storm, carrying signs and posters. The driving rain made it impossible to connect the public address system without risking danger, so the speakers' agenda for the march—including Senate Health Committee Chairman Tarky Lombardi, Jr, R-Syracuse, Assembly Health Committee Chairman James R. Tallon, Jr, D-Binghamton, and Assembly Minority Leader Clarence D. Rappleyea, Jr, R-Norwich—was cancelled.

Although the physicians could not communicate with the speakers directly, they did send a message. The crowd surged up the steps of the Capitol shouting, "We want reform and we want it NOW!" They continued chanting, shouting and banging on the doors for almost one half hour before the crowd dispersed. Afterwards, the damp but still determined physicians headed off for meetings with legislators and cups of hot coffee.

NEWS BRIEFS are compiled and written by Sandra Cirincione.

Defendant: A Psychiatrist on Trial for Medical Malpractice

By Sara C. Charles, MD, *and Eugene Kennedy. 230 pp. New York, Free Press, 1985. $17.95 (hardcover)*

The liability crisis is rapidly becoming to the 1980s what the oil crisis was to the 1970s: an intractable societal dilemma filled with facts and dire predictions. Almost weekly, it seems, newspapers print stories of malpractice tragedies. Medical societies and insurance firms counter with reams of statistics showing what the inexorable rise in liability insurance rates has done to the cost of medical care, and how the evolution of what *Time* magazine recently called a "Sue 'em society" has eroded the once sacrosanct physician/patient relationship. The media has brought us dozens of victims whose injuries, allegedly caused by incompetent medical care (never by sheer bad luck), make them short-time celebrities.

Now, in her book *Defendant*, Dr Sara Charles tells what it is like to be the physician-victim: "My first feelings after being charged with medical malpractice were of being utterly alone. Suddenly I felt isolated from my colleagues and patients. . . "

Dr Charles, a psychiatrist and associate professor of clinical psychiatry at the University of Illinois Medical School at Chicago, became embroiled in a five-year trial for malpractice. During the span of her experience she spoke with other physicians in similar situations and researched the subject. *Defendant*, written with her husband, Eugene Kennedy, a novelist and professor of psychology at Loyola University, is the result of her trial and research.

"Like everyone else," she writes in her introduction, "I was fully aware of the horror stories about patients who suffered from negligent doctors. Until I was sued, however, I had no idea that similar stories existed about doctors who had been involved in what they considered unjustified malpractice suits. I learned not only that large numbers of physicians felt isolated and ashamed of the compromises with their professional judgment that they made through practicing 'defensive medicine,' but that many had been permanently damaged as persons and practitioners by the impact of legal action in their lives."

The authors begin their tale by setting out a hypothesis—that unjustified malpractice suits exact a toll on medicine in America that its citizens may be eventually unable to pay. Next, they relate the story of Dr Charles' own trial, and, like good researchers and analysts, they then widen their scope to take in the problem as a whole.

The facts of the case are easy to relate: a client whom Dr Charles calls "Terry Walker" began a course of therapy with Dr Charles late in 1974. The young woman was beset with problems relating to her boyfriend, her career choice, and her establishing independence from her family. They met weekly and progress was made. Then, nearly a year later in mid November of 1975, Terry Walker climbed to the roof of her six-story apartment building and jumped off. She did not die, but her injuries left her confined to a wheelchair, presumably for the rest of her life. Dr Charles continued to see Ms Walker professionally at the rehabilitation center where she was convalescing until March. Then, in October of 1976, Dr Charles was served with a summons. She was accused "of being a negligent doctor, of being a careless and indifferent physician who had done grievous harm to Terry Walker." That summons began a five-year ordeal in which Dr Charles was sued for $10 million.

From the very beginning, as she read the complaint against her, Dr Charles found the situation described wholly unrecognizable. One section read as follows:

> The Defendant, a trained Psychiatrist and Medical Doctor, was negligent in her actual therapy sessions with the Plaintiff by not taking the Plaintiff's depression and suicidal tendencies seriously, joking about them, insulting and degrading and in other ways which only caused the Plaintiff to go into a deeper depression, to distrust her self-worth and ultimately to attempt to commit suicide.

The trial, described day-by-day, constitutes a valuable close examination of our legal system. It is a system, says Dr Charles, that by and large works: "I was grateful for the opportunity to have my case heard in court before a jury of average Americans, and the experience deepened my faith in the jury system and in the tight, highly disciplined court procedures . . . I believe that if more people, including accused doctors, saw their cases to trial and won them, fewer nuisance or frivolous suits would be initiated in the first place. In law, as in war, there is no substitute for victory."

During the course of her case, Sara Charles more than once reflected on the unfairness of the charges against her and said, "If I am found guilty of malpractice over this, I will never practice medicine again."

Dr Charles did eventually win her case, but she experienced no elation in her victory. There was still a sense of sadness and disruption. "I had wanted the truth to

emerge. That is different from wanting to defeat someone else. There had been too much pain for everyone to want any feeling of triumph. It is difficult to make sense of such an involvement, to see it whole, or to view it in a larger perspective of events, or to know whether one has grown or diminished because of it. What, a person must ask, is the point of this?

The courtroom drama, with its shifts of emotion and gradual illumination of what actually happened, is fascinating theatre and it makes up the bulk of the book. However, it is the answer that Dr Charles gives to her own question—what is the point of this?—that makes *Defendant* an important work.

In the third section of their book, Dr Charles and her co-author attempt to define the medical liability crisis. In chapters entitled "The Scope of Malpractice Litigation," "Medical Negligence: A Protean Concept," "A Generation of Malpractice Crisis," "Malpractice Litigation: A Crisis Getting Worse," and "Side Effects on Doctors and Patients," they examine the medical liability phenomenon from all perspectives, and they come to some important conclusions. They are not at all sure that physicians and attorneys or insurers can ever actually co-exist equally. "Lawyers," they point out, "are accustomed to the adversarial style of grave accusations trussed in legalese, and they do not make or take them personally. Insurers, whose public relations imagery depicts them as nobly and amiably dedicated to humanity, are basically businessmen who sell coverage for potential loss . . . Lawyers and insurers simply do not conceive of the world or interact with it in the same way physicians do."

Physicians, who, in the majority, possess obsessive-compulsive characteristics, says Dr Charles, "do take things personally, especially accusations that they have been negligent in their professional practice. So, too, they feel malpractice litigation as a referendum on their deepest selves." But then, "Lawyers do not perceive [medical malpractice] along with the public as an essentially moral issue." In fact, most lawyers feel that their commitments end with the conclusion of the trial they are involved in, win or lose. "Trial lawyers, no matter how dramatically they make a case against physicians in court, do not seek to have the latter's licenses taken away or have them barred from practice."

This indifference of attorneys brings the authors to their major conclusion; that physicians have looked in the wrong place for a solution to the malpractice crisis. In a personal communication to this reviewer Dr Charles wrote the following:

> "The major players in the malpractice litigation situation have been insurers and lawyers until very recently. Doctors have been beating their breasts, acknowledging that there are indeed 'bad' doctors out there and turning the problem over to lawyers and insurers to manage. As a result we have had legal and insurance solutions—neither of which work."

This thought is amplified in the chapter, "Malpractice Litigation: A Crisis Getting Worse," in which the authors trace the changing and broadening concept of medical negligence from strict liability to "an effort to guarantee compensation, irrespective of fault, for people suffering because of the multiple hazards of modern life," including adverse outcomes in medical treatments. This widening definition opened up a pool of money that has been fought over by, essentially, two groups: lawyers and insurers. Lawyers try to widen the definition further, to protect their individual clients (and, yes, to increase their own fees); and insurers try to keep the definition narrow, to better predict risk (and thus assure profits).

Says Dr Charles (personal communication):

> "The competing interests of law and insurance have merely moved their continued struggle with each other onto the grounds of health care. Lawyers' lack of interest in removing allegedly negligent doctors from practice can be explained simply: their concern is primarily with compensable mishaps than with the probity of medical care. The willingness of insurance companies to write higher premiums for allegedly malpracticing physicians merely reflects the nature of their business: to cover risk, irrespective of moral, ethical, or other considerations, at a cost."

This battle, says Dr Charles, has eroded the quality of health care in the United States. Already altered are the delivery and nature of health care, not only through increasing costs, but more subtly through the emotional reactions of physicians who, though vindicated in court trials, find that they can no longer practice with confidence or derive much satisfaction from their occupation. She gives several examples of this in *Defendant:*

> One could cite the cardiovascular surgeon, an inventive pioneer in his field, who, even though cleared of negligence charges, found that the possibility of their being lodged against him again without justification made further practice impossible. At the height of his career he retired to become a gentleman farmer, his irreplaceable knowledge and expertise removed from the spectrum of health care.

The authors cite others affected, note the essentially experimental way medicine (or indeed all science) progresses, and conclude that the "attenuation of health care and medical research that is already occurring in the United States leaves ordinary people as the ultimate bearers of the losses that flow from these events."

What can be done? Dr Charles maintains that insurance solutions and legal solutions have not and will not work. There must be a medical solution (that is, a treatment that physicians can administer and control themselves). In her book, Dr Charles points out:

> The massive engagement between insurance and law in which organized medicine has become so expensively involved has been aimed at making doctors insurable and legally defensible, neither of which outcome is essentially relevant to whether or not they are good doctors.

How may physicians raise the consciousness of the public, so that a "medical" solution can be tried? Dr Charles has been thinking about this problem since the publication of her book. At present she is preparing an expanded and revised paperback edition to be published this autumn. In a personal communication, she expressed some of her thoughts:

> "What doctors have to do is communicate to the public the mission of medicine and what it is really like to practice medicine. It is inherently stressful, dealing with life and death issues, split second decisions, tension-filled and full of ambiguities. It is an

essentially human and therefore imperfect endeavor. Doctors have to communicate this to the public so that there is a much better understanding of medicine's possibilities as well as the fact that a poor outcome can occur despite the most competent efforts of a physician."

Whether or not one agrees with them, Dr Sara Charles and Eugene Kennedy have produced a book that is rare in its honest effort to examine both a personal and a public crisis in a thorough, open, and even-handed manner. The book is must reading for physicians, patients, and social historians of the late 20th century.

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Confronting the Malpractice Crisis. Guidelines for the Obstetrician-Gynecologist

Edited by Daniel K. Roberts, MD, Jeffrey A. Shane, MD, and Margaret L. Roberts. 304 pp. Kansas City, KS, Eagle Press, Inc, 1985. $50.00 (hardcover)

In this book, a group of lawyers and physicians from various sectors of the country have pooled their information together to help obstetricians and gynecologists confront the malpractice crisis. In so doing, they have produced a valuable and highly readable volume.

A necessary aid to understanding this book is a thorough study of the mechanisms of malpractice litigation. "Adequate knowledge and familiarity with our legal system will remove the fear of the unknown, allow a thorough appraisal of the case, permit continued physician involvement in the legal process, bring about smaller settlements for meritorious cases, reduce costs, and ultimately provide an equitable system for both patients and physicians." In saying this, the authors set forth the major theme of the book.

The physician and the lawyer have different backgrounds. The physician is trained in anatomy, physiology, bacteriology, and pathology and organizes the four sciences to fight and treat human disease appropriately. The lawyer, however, has a far different training. He deals with words and facts and the interpretation of what is right and wrong. The more the physician understands the legal profession, the less frightened he becomes. This book was written to give the physician insight into what the lawyer seeks in the way of relevant and irrelevant information concerning malpractice litigation.

From 1975 to 1976, the medical malpractice crisis was exacerbated by a tremendous rise in major insurance carrier fees. In the pivotal states of New York and California, the fees rose 200% and 300%, respectively. These same rate increases affected hospitals; some large facilities had a rise in insurance rates of greater than $1 million.

Patients have gradually been learning more about their health care and as their knowledge grew, more malpractice cases have resulted. By the procedural rules of law, the appellate court system gave plaintiffs easier access to the courts. There was also a tendency for juries to award large damages caused by negligent care. Although the funds awarded in such suits arise from insurance money, they actually originate from the patients.

As the private insurance companies went into bankruptcy, more mutual malpractice insurance companies appeared, in which the physicians developed their own protective organizations. Some states have also set up arbitration pre-trial panels that review the cases. In order to protect themselves, some hospitals have organized risk management programs; Florida requires that all hospitals set up such a program. These programs seek out physicians who are the principal offenders in malpractice incidents and, on occasion, remove multiple offenders from the staff of the institution.

Early on in this book, it is explained that a tort is a civil wrong. A breach of contract may be corrected by an action for damages. This law reverts back to the Code of Hammurabi. If a physician at the time of the Babylonian kings caused the death of a patient, his hands would be cut off.

American law can be traced back to the year 1200, two centuries after the Norman conquest of the British Isles. The common law was brought to the United States by the early colonists. Historically, all wrongs were considered against the crown and were classified as felonies of crimes of trespass. Negligence crept into the law as a separate and distinct tort. This concept was not applied in this country until the 1800s. Medical negligence is considered that care falling below the standards set up by the average physician in the community. Negligence is defined as a patient placed under unreasonable risks. A negligent act causes injury; the plaintiff therefore suffers unreasonable damage that may be measured in the loss of money.

The authors then explain the sequence of events of a lawsuit and provide useful advice. When a lawsuit is begun by a patient, the physician should notify the insurance carrier. A lawyer is then chosen by the carrier to defend the physician. The plaintiff files a formal complaint, which is officially known as a summons. The defendant and his attorney prepare a written response that may either deny or admit some of the allegations contained in the complaint. At this point, either side may suggest settling the case.

The merits of any case may be decided in the amount of damages that the plaintiff has sustained. The limits of the liability policy may also be included. If a case is not settled, a date is then set for the trial. Each lawyer, both for

the plaintiff and the defense counsel, has an opening and closing statement that summarizes the important facts in the case. Each lawyer may cross examine expert witnesses. The judge then instructs the jury on relevant legal principles. The jury reaches a verdict and then presents it to the court. The verdict may be appealed or a countersuit may be instituted. Sometimes the truth does not turn the verdict; rather, the way the lawyers run their section of the trial may be more significant.

The principal actor in the medical drama just described is the physician, who is the defendant in the case. As the authors observe, if he enters the courtroom with much emotion, frustration, and hostility against his previous patient, he then assumes a negative image that may result in his losing the case. The plaintiff has initiated the suit because he or she assumes an error has been made by the physician and is seeking monetary compensation. Although the physician may be shocked to know that the former patient has brought about the suit, he or she must remain calm and composed in order to explain the medical events of the case.

Another important aspect of the medical drama is the presence of the insurance carrier. The physician should know the limits of his insurance policy and whether the company would prefer that he settle early or later.

Expert testimony is often a source of anxiety for the physician as defendant in a medical malpractice suit. At times, the same experts may testify for both the defendant and the plaintiff; it is usually dependent on who can come up with a larger fee. The judge controls the court during litigation, and points out the rules of law to the participants and, primarily, the jury. Although judges are well trained in the legal aspect of litigation, they frequently have little experience in the specific aspects of medical judgment. Therefore, the individual providing the expert medical testimony often has the ability to influence both the judge and jury. An expert witness well versed in the subject matter reduces injustice and partiality.

The jury consists of lay persons, most often without medical backgrounds, and of varied outlook and education. There are six jurors in federal court and 12 in district court.

In the next section of the book, the authors discuss cross examination. Cross examination scrutinizes the subject matter presented in the case; the leading questions are carefully phrased, often to make the witness agree with the lawyer. This method of questioning may strengthen witnesses' testimony on controversial subjects. However, by questioning a witness' character, an attorney may succeed in contradicting the witness' credentials. On occasion, when the results of cross examination are presented to a witness, a faulty memory of acts may result in the entire testimony being subject to question. This may cause the witness to be discredited by the jury.

The authors also discuss how the physician as defendant should act during litigation. There are certain guidelines to follow in order to best present oneself during court proceedings. The defendant should not appear frustrated, anxious, or angry with the plaintiff; he should only answer questions that are asked without volunteering additional information. As with any professional, the physician should remain calm and composed. The authors rightly emphasize that the communication should be confident, with simple language that the jury can comprehend.

Res ipsa loquitur literally means "the thing speaks for itself." This legal truism was developed from a doctrine in the case of *Ybarra v Spangard* decided by the Supreme Court of California in 1944. Three conditions apply to this ruling: (1) The accident and the injury occur because someone is negligent. (2) The impairment must be under the exclusive control of the defendant. (3) The plaintiff plays no part in the misdeed. This doctrine may be applied when foreign objects are left in the body after surgery. If complications of a surgical procedure occur that follow with appropriate good standards of care, the plaintiff and his lawyer will be required to prove by expert witnesses that a breakdown in judgment intervened.

Informed consent is a crucial part of any malpractice controversy. The physician is expected to explain in detail the surgical procedure in a reasonable manner in uncomplicated language. The risks, complications, and likely outcome for the patient should be simply stated and all questions must be answered. If complications occur that were not discussed, the details must be recorded and the patient, if understanding, should be aware of the problems as soon as the surgical procedure is terminated.

The best defense against malpractice in the field of obstetrics and gynecology, as clearly stated by the authors, is to practice the best medicine possible. Such outstanding care must be represented by excellent medical records and documents of all tests performed. After a case has begun, medical records may not be altered. Tampering with medical documents is unethical and provides grounds for a liability suit for the vulnerable physician. The authors advise that when practicing medicine, be optimistic that your mode of treatment will cure the patient.

There are few areas of medicine as open to malpractice as the field of obstetrics. A careful history and physical examination may prevent certain high risks. If there is a family history of Down's syndrome, or if any other congenital anomalies appear in the family history, the patient should be seen by a genetic counselor and undergo amniocentesis and chromosomal analysis. The fetal heart monitoring record should be safeguarded indefinitely for possible use many years later in court. Types of analgesia and anesthesia should be documented and individuals who are competent in cardiopulmonary resuscitation should always be available.

The brain damaged child is most often the best case to win a major verdict. As science progresses, many of these cases of brain damage are not caused by a physician's negligence. There are many specific causes that are not related to obstetrical care. Karyotype is performed to eliminate the presence of chromosomal abnormalities. Metabolic studies may exclude inherent metabolic disease. Computed tomography and EEG may help to reject the presence of central nervous system pathology. The child development evaluation for hearing, sight, and speech may provide information to prove that the disease or injury predated delivery. Cerebral palsy and other diseases that occur prenatally may also be the cause of the injury. In order to find the clinical disease entity, neurologists and geneticists are important figures to bring into a trial; these specialists are frequently able to distinguish a cause for injury

that is unrelated to labor.

The book contains a thorough discussion of risk management and loss prevention, which are essential in a hospital's quality assurance program. Risk management committees review previous cases and attempt to find those physicians responsible for the malpractice. Once the risks are identified, control techniques and proper insurance financing may help to decrease the probability for future liability suits. A risk manager is usually a physician/administrator who develops knowledge about legal issues and insurance. The risk manager should participate in grand rounds of each department so he has a good understanding where medical care may be slovenly, unconcerned, or careless. A board of trustees may also participate in gathering malpractice information to determine the magnitude of the institution's losses associated with inefficiency and negligence. It is advantageous for a large-sized hospital to have a single medical staff committee for coordinating quality assurance and risk management efforts.

Next the authors delve into issues related to radiation and imaging. The public has become increasingly aware of the potential hazards of radiation. The ideal time to perform radiologic studies on a woman in the childbearing period is the first ten days of the menstrual cycle. Radiographic pelvimetry is no longer performed in large institutions; pelvic examination during labor substitutes for the previous radiographic pictures. If a child develops leukemia because of pelvic radiologic exposure, the obstetrician may be held liable. Radioisotopes are contraindicated in pregnancy and in the second half of the menstrual cycle. If radiographs are essential for diagnosis, the scatter radiation should be reduced to a minimum by wearing a protective apron. If a fetus has had unnecessary irradiation, teratogenic, carcinogenic, and growth retardant effects may result. Guidelines are available for reducing irradiation to the pregnant woman and limiting exposure to the first half of the menstrual cycle.

Ultrasound may be considered the most important advance in the specialty of obstetrics in the past half century. There is no concrete evidence indicating that it is harmful to the mother or fetus. Sonography may detect congenital anomalies of the fetus and the uterus, separation of the placenta, placenta previa, polyhydramnios, and oligohydramnios, and provide a rough estimation of the size and age in weeks of the fetus. Ultrasound should be performed by adequate technicians and interpreted by well-trained ultrasonographers. Continued education of the new techniques permits technicians to keep informed and well versed on the advances in ultrasound. A knowledge of the legal implications of any new technique such as ultrasound is imperative both for the physician who orders the examination, and for the technician who performs the test.

The subject of in vitro fertilization and egg transfer has recently arisen in malpractice suits. Initially developed by Edwards and Steptoe in Cambridge, England, this procedure is now being performed in the United States. Eggs are collected by laparoscopy or direct puncture through the bladder or vagina. Fertilization of the oocytes occurs in vitro and the eggs are transferred to the uterus at various stages of growth. Ectopic pregnancies may result from an in vitro attempt, which may provide liability for the institution at which the procedure was performed.

The United States Supreme Court ruled that all persons have the privilege to procreate. Therefore, in vitro fertilization should be privately undertaken and also constitutionally protected. However, some opponents believe that a fertilized egg is a human being and if failure to implant occurs, it should be considered murder. Informed consent on the part of husband and wife should be completed prior to the procedure being initiated. If a child is born with a defect, a law suit may be instituted; chromosomal analysis and careful sonography should be routinely performed to detect abnormalities.

The use of donor oocytes with the recipients' husbands' sperm or donor sperm is now occurring with increasing frequency. This process is instituted when the recipient lacks ovaries, if her ovaries are inaccessible, or if premature menopause occurs. The ovulatory cycle of the recipient may be synchronized with the donor; fresh embryos or deep frozen embryos may be thawed and transferred at the correct time of the cycle. If the infants are born with abnormalities, the physician may be proven negligent and heavy damages may result. If a woman has no uterus or an abnormal uterus, or wishes not to participate in pregnancy, a surrogate mother may intercede. A great deal of the development of the infant is dependent on the maternal environment. Many people believe that surrogate motherhood is not in the best interest of society. Physicians and lawyers should make the parties aware of the potential problems of surrogate mothers. The law codes have not been written to protect the unborn child against selection and consent for donor oocytes, sperm, embryos, and surrogate childbearers.

In 1974, the State of California attempted to analyze the potential claims and injuries occurring throughout the state. The California Medical Insurance Feasibility Study included all alleged negligence cases occurring in the state. Potentially compensable events were divided into the following categories: minor and major temporary disabilities; minor and major permanent disabilities; grave permanent disabilities; and death. There were 3,011,000 admissions to nonfederal general hospitals in California in 1974. Potentially compensable events resulted in 140,000 cases; 80% (112,000) were minor disabilities that were immediately reversible. Substantial functional disabilities were expected in 5,200 cases (3.8%). The final figure placed 23,800 patients as sufficiently disabled to seek compensation. The confidentiality requirements did not allow the study to determine the number of persons that sought lawyers and went on to present a suit to the defending physician.

The editors and contributors to this excellent text have clearly and thoroughly covered all of the relevant issues concerning malpractice as it affects obstetricians and gynecologists. They have produced useful guidelines that will be of help not only to those in this specialty but to all practicing physicians.

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Pogo, Brahms, medical malpractice, and common sense

Medical Malpractice: A Preventive Approach

By William O. Robertson, MD. 222 pp, Seattle, WA, University of Washington Press, 1985. $20.00 (hardcover)

Medical Malpractice: Theory, Evidence, and Public Policy

By Patricia M. Danzon. 264 pp, illustrated, Cambridge, MA, Harvard University Press, 1985. $25.00 (hardcover)

"We have met the enemy and it is us," said Pogo. For all us aficionados of the lovable 'possum from the old Walt Kelly classic comic strip, we can add "amen."

And what does Brahms have to do with Pogo and medical malpractice in general, and medical malpractice book reviews in particular? Equal parts of patience, perseverance, experience, and poetic license will hopefully help us make the necessary connection. According to musical folklore, when young Brahms wrote his First Symphony, he broke the rules by introducing a new theme at the end of the symphony, and blatantly having it blasted out by a trumpet, no less. And, to add insult to injury, this new, misplaced theme was very reminiscent of Beethoven's Ninth Symphony. Brahms allegedly stated that while anybody could hear the similarity, it took an understanding, intelligent person to know, understand, and appreciate the differences.

Pogo and Brahms in their own ways stated simple truths. We are our own worst enemy. We tend not to recognize simple truths and are lacking in the problem-solving ability to understand these basic truths. These statements are, perhaps, too harsh. But so is the current malpractice crisis—and a crisis it is and will continue to be until proper efforts are made to understand and combat medical malpractice. The medical profession will remain its own worst enemy unless and until its attitude, thinking, and efforts change in the right direction.

I remember arguing with a hospital staff member because something was noticed on the chest x-ray taken on admission of a patient who entered the hospital for treatment of a urological problem. Immediate repeat and special x-rays were ordered and insisted on before the patient was discharged from the hospital. Requests, pleas, and arguments to move quickly before the patient's discharge were to no avail. I got my way by going directly to the radiologist, who, fortunately, was sympathetic. He understood the medical-legal need for immediate follow-up x-rays. I was bawled out by one of the administrative physicians for arguing. When the same administrative physician was asked if he wanted to know why I was arguing this matter, his answer was a curt and resounding, "No—it makes no difference."

But, in reality, it made a big difference, especially to the most involved and innocent of all parties in this matter—the patient. The follow-up x-rays—which were evaluated by a pulmonary consultant brought in pursuant to these new x-rays—raised the ugly spectre of an early lung cancer. The patient and family, unaware of the behind-the-scenes in-fighting, were duly impressed and appreciative. The hospital and its staff came up smelling like a rose for their acumen and dedication. The administrative physician, like Brahms' supposed detractors, only heard the noise of the argument, but did not want to know why the noise took place. Any person—even one without prior medical training—could have recognized an argument.

The correct attitude and proper reaction on the part of a physician should have been to want to know the why behind the argument. In many ways this, in microcosm, is what the malpractice crisis is about. Too many hospital personnel, administrators, and physicians see and hear the battle, the noise, and the fallout. However, not enough of them seem to care or want to know the why behind the crisis, leaving themselves exposed to potential risk. As Santayana, the philosopher, once said, those who do not learn from history are doomed to repeat it. Perhaps this is why the malpractice crisis continues to escalate. In the actual example given, not only would the innocent patient have suffered, but the hospital and the doctors involved would have suffered as well.

Who and what is out there in the medical malpractice wilderness that we can look to for succor, aid, and practical help? In general, there are the usual defense lawyers, lawyers representing the hospitals, and local and national medical societies. And, not to be forgotten is our own common sense, which should not be allowed to vegetate, disintegrate, and atrophy from lack of use. In particular, however, there are two recent books on malpractice—each one of which is valuable in its own right—which, when read and used together, nicely complement each other.

In the first book, *Medical Malpractice: A Preventive Approach*, Dr Robertson also quotes Walt Kelly's Pogo saying, "We have met the enemy and it is us," in his discussion on expert witnesses. So already I have found a kindred soul.

Dr Robertson's credentials are impressive; his book is equally so. He is head of the Washington State Medical Association Risk Management Program, director of the Quality Assurance Program at Children's Orthopedic Hospital and Medical Center in Seattle, Washington, and professor of pediatrics at the University of Washington. He brings an impressive array of experience into the field through this book.

Dr Robertson aptly recognizes medical malpractice problems for both the patient and the physician. He uses case studies to their fullest teaching potential and identifies eight major areas of high-risk litigation using case presentations: surgical complications; pregnancy and birth; drug prescription and its use; diagnostic failure; overprescribing; failure to explain and obtain informed consent; errors in documentation; and communication breakdowns. In addition, the author presents a valuable, easy to use appendix containing 30 topics on risk manage-

ment, including emergency room discharges, drug usage review, staff by-laws procedures, surgical reports, incident reports, terminating life-support systems, altered records, lawyers' requests for hospital records, verbal orders, incident report follow-ups, and consultation notes.

This easy to read book is valuable for members of both the medical and legal professions. With regard to my own story about the administrative physician, Dr Robertson's chapter on "Doctor-Patient Communication" deals not only with communication problems between physicians and patients, but also those between physician and physician as well as physician and nurse. The book discusses many other problems, real and anticipated, that the physician will probably see in the practice of medicine. If digested and followed, the book is chock full of advice on how to avoid medical malpractice suits. It also contains helpful advice for the medical profession in general, the practicing physician, and the hospital and its staff in recognizing the dangers of potential medical malpractice risks and suits. Fortunately, Dr Robertson is not alone in recognizing and pinpointing both potential and actual medical malpractice pitfalls and problems.

The second book, entitled *Medical Malpractice: Theory, Evidence, and Public Policy*, goes beyond mere lawsuits and delves into the ramifications for society of what often may be a needless internecine battle of professionals in the medical malpractice arena. Danzon, an economist, is an associate professor at the Center for Health Policy Research and Education at Duke University. Her book is a scholarly approach that deals with the details and dictates of the cost (financial and emotional) effectiveness of the liability insurance system.

Danzon essentially divides her book into three parts. In the first part she develops a theoretical framework for evaluating the existing malpractice-tort system and its proposed reforms. The second part examines issues in malpractice insurance, and the third section discusses various reform proposals and alternatives to the medical malpractice system. Professor Danzon discusses ways of deterring malpractice, compensation to injured parties, as well as the extension of liability and, unfortunately, the growing malpractice risk. What should strike physicians as ominous is that malpractice claims and their consequent costs are continuing to increase in spite of the reforms that have already been enacted.

Professor Danzon discusses the malpractice system from the points of view of the law, the insurance business, and the effects of medical malpractice on the general public. She makes us aware of the cost effectiveness of deterring malpractice and she describes compensation to the injured parties. She analyzes the insurance markets and current malpractice claims in order to develop a practical basis for effective reform proposals.

This is a carefully detailed book, replete with valuable information and citations that make it must reading for serious students of the current medical malpractice crisis. The audience should include lawyers interested in medical malpractice defense and physicians.

Whereas both books are extremely appealing to members of both the medical and legal professions, Dr Robertson's book would appeal more to the practicing physician, and Professor Danzon's book would appeal more to the researcher, legislator, and judge. Together, these books represent formidable weapons in the arsenal of medical-legal defense, providing facts, evidence, and collections of previous cases. If the lessons that can be gleaned from these volumes were put to practical use, then perhaps the enemy will stop being us, and we will start to truly understand the meaning behind all the music and the noise.

It is a pity that these books were not written 20 years ago. But then, 20 years ago there was no pressing need for them. Necessity remains the rightful mother of invention.

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Aug 11–15. **Occupational Health and Environmental Radiation Protection.** Info: Office of Continuing Education, Department A, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115. Tel: (617) 732-1171.

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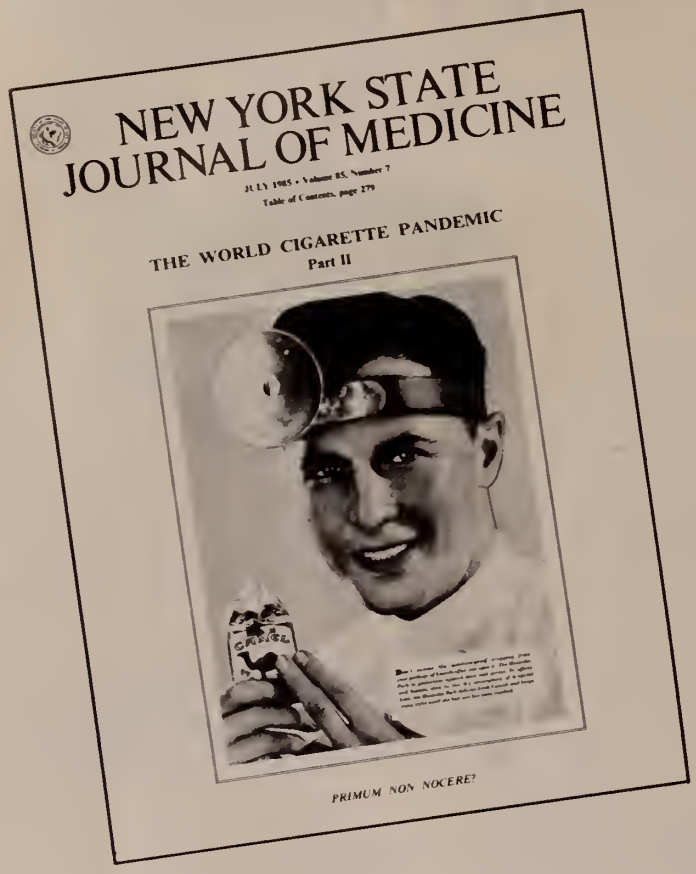

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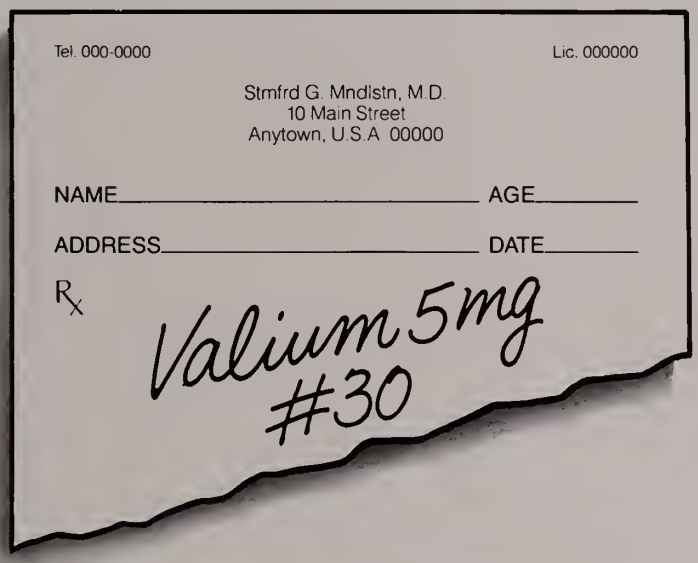

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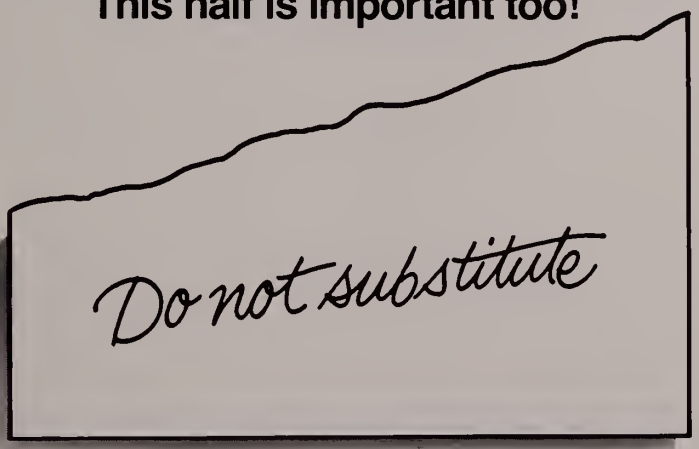

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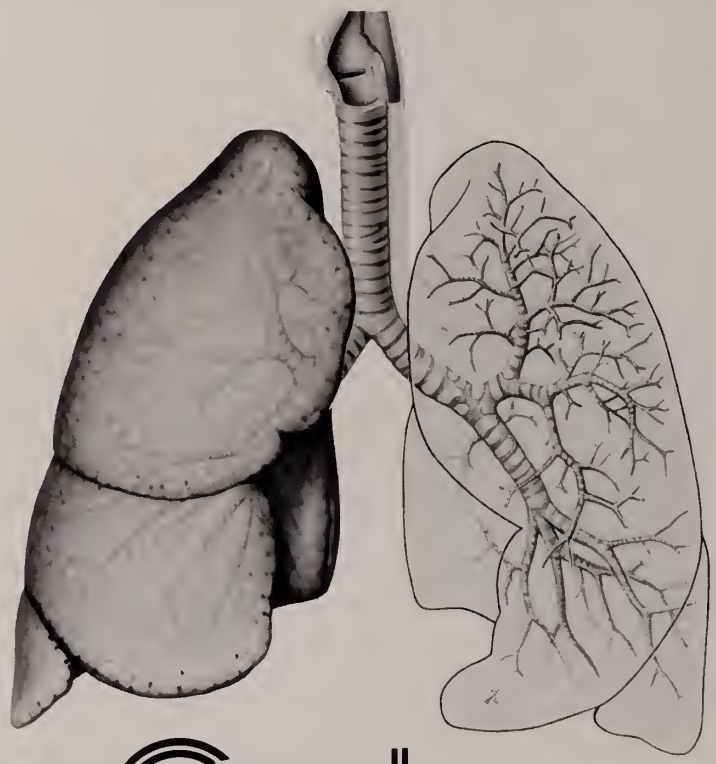

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Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- In renal impairment, safe dosage of Ceclor may be lower than that usually recommended. Ceclor should be administered with caution in such patients.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
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- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%.

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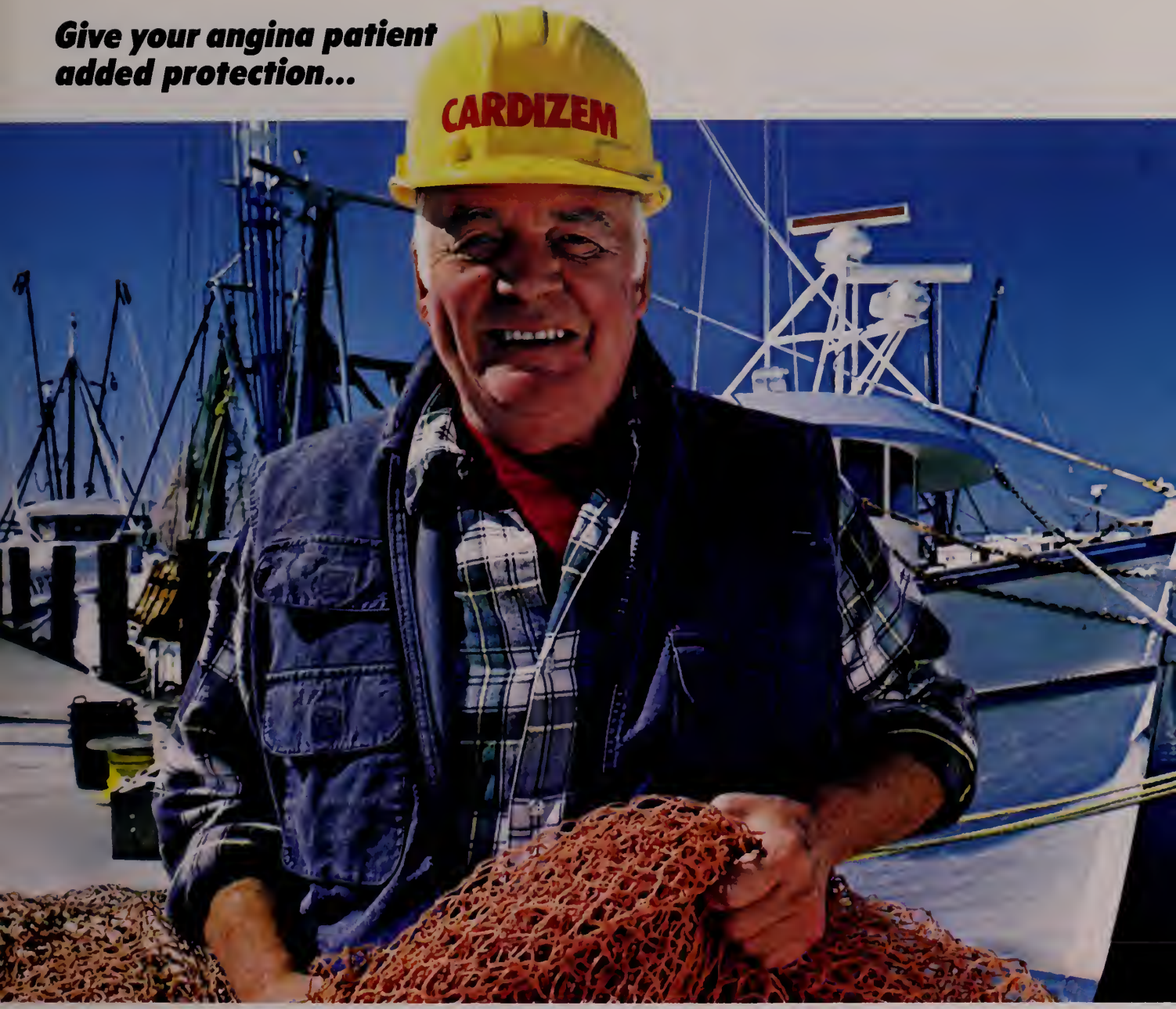

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CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction 24% ± 6%) showed improvement in indices of ventricular function without significant decrease in contractile function (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. Issued 11/85

See complete Professional Use Information before prescribing.

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SEPTEMBER 1986

AROUND THE STATE

MANHATTAN

Sept. 3. **Alternative Delivery and Financing Systems: Your Options and How to Evaluate Them.** Info: Registrar, American Medical Association, Department of Practice Management, 535 N Dearborn St, Chicago, IL 60610. Tel: (312) 645-4958.

Sept 3–5. **New Concepts in the Management of OB-GYN Infections.** Grand Hyatt Hotel. Info: Program Coordinator, SUNY Upstate Medical Center, 750 East Adams St, Syracuse, NY 13210. Tel: (315) 473-4304.

Sept 11–14. **Cardiopulmonary and Critical Care Medicine.** 23 Cat 1 Credits. Grand Hyatt Hotel. *Sept 20–21.* **Clinico-Pathological Conference About Melanocytic Neoplasms.** 13 Cat 1 Credits. Grand Hyatt Hotel. *Sept 29–Oct 3.* **Five Day Emergency Medicine Board Review Course.** 29 Cat 1 Credits. NYU Medical Center. Info: Registration Office, NYU Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Sept 23. **Update on Coronary Risk Factors.** New York Helmsley. Info: New York Cardiological Society, 84 Grove St, Suite 2, New York, NY 10014. Tel: (212) 924-5346.

NASSAU

Sept 10–12. **6th Annual Advanced Course in Lower Limb and Amputation and Prosthetics.** 17½ Cat 1 credits. Info: L. W. Friedmann, MD, Department of Physical Medicine and Rehabilitation, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-2522.

Sept 13. **The Poisoned Patient, Emergency Toxicology.** 6 Cat 1 Credits. Info: Howard Mofenson, MD, Poison Control Center, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-2323.

Sept 19. **New Dimensions in Anxiety Disorders, 1986.** 4 Cat 1 Credits. Info: Hugo S. Kierszenbaum, MD, Department of Psychiatry and Psychology, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-2511.

Sept 26. **Depression and Suicide in Children and Adolescents.** 7 Cat 1 credits. Rust Auditorium. Info: Mary B. Strong, Department of Health Education, North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030. Tel: (516) 562-3045.

WESTCHESTER

Sept 24. **Breast Cancer—Therapeutic Dilemmas.** 6 Cat 1 credits. Cedarwood Hall Auditorium. Info: Office of Continuing Medical Education, NY Medical College, Valhalla, NY 10595. Tel: (914) 993-4487.

ALBANY

Sept 29–30. **Birth Defects Symposium XVII.** Albany Hilton Hotel. Info: Ann M. Willey, Wadsworth Center for Laboratories and Research, NYS Department of Health, Rockefeller Empire State Plaza, Albany, NY 12201.

BUFFALO

Sept 5. **Alternative Delivery and Financing Systems: Your Options and How to Evaluate Them.** Info: Registrar, American Medical Association, Department of Practice Management, 535 N Dearborn St, Chicago, IL 60610. Tel: (312) 645-4958.

Sept 20. **Update of Controversies of Gynecologic Malignancies.** Info: Gayle Bersani, Roswell Park Memorial Institute, 666 Elm Street, Buffalo, NY 14263. Tel: (716) 845-2339.

SYRACUSE

Sept 5. **Alternative Delivery and Financing Systems: Your Options and How to Evaluate Them.** Info: Registrar, American Medical Association, Department of Practice Management, 535 N Dearborn St, Chicago, IL 60610. Tel: (312) 645-4958.

AROUND THE NATION

CALIFORNIA

Sept 2–5. **2nd Annual Physics and Biology of Radiology.** 28 Cat 1 credits. Town and Country Hotel, San Diego.

Sept. 12–14. **Sonographers' Update and Review.** 20 Cat 1 credits. Info: Dawne Ryals, Ryals & Associates, PO Box 920113, Norcross, GA 30092–0113. Tel: 1 (404) 641-9773.

Sept 3–5. **Pediatric Trauma 1986—Practice and Controversies.** Hotel Inter-Continental, San Diego. Info: Unconventional, Inc, PO Box 33185, San Diego, CA 92103. Tel: (619) 692-9115.

Sept 8–12. **Clinical Magnetic Resonance.** 30 Cat 1 credits. Hyatt Regency Hotel, San Francisco. Info: University of California, Room 569U, San Francisco, CA 94143–0766. Tel: (415) 666-5808.

(*Continued on p 9A*)

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COMMENTARIES

Emergency medical services in the 1980s

The roots of emergency medical services (EMS) are buried deep in history. We have progressed far along the same dusty road on which the Good Samaritan[1] of old laid the foundations for the philosophy of modern emergency care. Little did he know he would also lay the foundation for many a legislative debate. But the medical world of that Good Samaritan was simpler. He did not have to worry about a Quality Assurance Committee reviewing whether his handling of the patient's injury at the roadside was appropriate and in keeping with community standards. Who was to say that oil and wine were effective wound dressings? Was the donkey he used up to Department of Transportation specifications? And should he have transported the patient to the nearest inn, or should he have bypassed it and gone to a Level I inn that was farther down the road but perhaps better equipped to care for trauma? Did the outcome justify the time the Good Samaritan took at the scene to bind the poor man's wounds and to apply the oil and wine, or should he have "swooped 'n' scooped?" Who said the Good Samaritan did a good job anyway?

Alas, the "Good Samaritans" of today's emergency medical services have a lot more on their minds than our hero of biblical stock. Although the roots of EMS run deep and its heritage is a proud one, as a system it is but a fledgling in the nest of medicine, with only 20 years' experience on which to base decisions as to its future. Mustalish,[2] in his excellent review of emergency medical services in this issue of the *Journal*, outlines the major political, social, and economic factors and events that contributed to the development of modern prehospital (EMS) care systems. Evident in his outline is the gradual growth over two decades of public support for prehospital care, the resultant investment of public monies to design and study systems, and the recent phasing out of federal support. Sounding a rather sullen note, Mustalish warns that the loss of funding may well slow or even reverse the progress of the last two decades.

Although there is little doubt that the loss of government funding and leadership at the federal level will adversely affect the further growth and refinement of emergency medical services, this is not the greatest disaster that could befall the descendants of the Good Samaritan. Indeed, when faced with the loss of state or federal dollars, communities rally around the EMS banner and consistently support local governmental and tax-based funding to keep ambulances on the streets. The most challenging problems facing EMS systems today concern clinical questions and debate over the value of EMS systems to patients.

Criley and colleagues[3] have defined several periods in the history of cardiopulmonary resuscitation (CPR) research: an initial era of discovery; then one of skepticism; then of acceptance and complacency; and the most recent era of rediscovery and refinement. The two-decade history of EMS has parallelled that of CPR, but the most recent period—the 1980s—might be considered a rebirth of the era of skepticism, and perhaps of refinement as well.

Those in EMS have come to the point during the past two decades at which it is necessary to sink or swim. The era of fast and easy federal funding is past, and we are now being asked to prove our worth or get out of the business. In short, the honeymoon is over.[4] Although the initial reaction to all of this may be to sound the sirens and draw the wagons in a circle, I believe the current era of skepticism is an exciting and healthy one. We must now prove that what we are doing is of medical value or continue, in some cases, to play games in the sandlot.

During the past two decades, the rapid growth of EMS systems has necessitated the development of a new breed of paraprofessionals who have taken their places in the trenches beside physicians and nurses as caregivers in the health system. The modern Emergency Medical Technician (EMT) and paramedic have stamped their personalities on the EMS system and have made their contributions to its development. They are here to stay. However, discomfort arises among physicians when it is realized that prehospital care workers, even as physician-surrogates, are employed by agencies that are often not part of

the medical care system and are not answerable to medical audit and review. If it is not time to put the "medical" back into EMS, then it at least needs reemphasis.

The delivery of emergency care in the field must be considered an extension of hospital and physician services. Control over patient care must be exercised by physicians skilled and trained in EMS, who have an ongoing relationship with prehospital care workers, and who carry the burden of responsibility for the care given in the streets.

Advanced life support largely began in the United States as pilot projects carried out by physician researchers who were attempting to duplicate the results of Pantridge in Belfast.[5,6] His mobile coronary care ambulance introduced the prospect that patient outcome could be bettered if early care were given in the home or on the street. His plan was a simple one; he merely loaded his coronary care unit (CCU) team aboard a standard ambulance stationed on the hospital grounds, and they sped off to treat the patient at home, prior to a somewhat leisurely ride back to the hospital.[5,7] It was, in essence, a modern form of the housecall.

The approach to the problem was somewhat different in the United States. The Viet Nam war supplied to the public safety agencies and hospitals of this country a cadre of well-trained corpsmen who were eager to apply their medical skills to civilian practice. There was, however, no ready outlet for their talents. The development of EMS services, especially within the fire service, offered this group the potential to use their training as the basis for an attractive career. In America, the attempts to emulate Pantridge used the concept of physician-extenders or physician-surrogates as providers of care. It was assumed that these non-physicians could be trained to carry out the procedures required to stabilize the patient and then transport the patient to the hospital. These prototype systems, developed in Seattle,[8] Miami,[9] and Los Angeles,[10] were closely controlled and evaluated on a day-to-day basis by the physicians who developed them.

With the growth of EMS in the 1970s, the medical experiment became medical practice, rather than mere experimentation. Important to this transition were the influence of television and the change in public perception brought about by the media. Gradually but surely, medical control of EMS systems was lost, and was passed to those beyond the perceptive probing of Quality Assurance Committees, M&Ms, rounds, and review conferences so tightly woven into the fabric of modern medical practice.

Little wonder, then, that the glitter soon faded and the harsh reality of caring for very sick patients began to wear through. We find ourselves in the 1980s confronted with a medical care system that, in some instances at least, has little medical accountability. The variation in this medical accountability and competent physician control has led to a resurgence of the great debate of "swoop 'n' scoop" versus "field stabilization."[11] The present state of EMS affairs prompts some observers to reject the expansion of advanced life support capabilities as currently configured.[12,13]

How did we arrive at this point, and where do we go from here? The loss of tight medical accountability in the late 1970s saw a continuance of the rote application of "cardiac-flavored" protocols to all sorts of patients, particularly the seriously injured. The theory of "field stabilization," so successfully demonstrated in the Seattle[8] system, began to be applied to even those patients who, by virtue of their injury or illness, had a time-dependent outcome.[14] For these patients, stabilization at the scene could not have succeeded, and the goal of prehospital care should have been the reduction of the time to receive definitive care. This element was demonstrated to be the crucial factor in determining outcome in the seriously ill or injured patient.[14,15]

With the recent interest in trauma and the development of regionalized systems for the care of the seriously injured patient, the role of prehospital care has come under closer scrutiny. For treating certain patients, the EMS system was weighed in the balance and found wanting.[16,17] Others described the success of advanced life support methods in the field applied to trauma patients.[18-21] Unfortunately, the comparison was of apples and oranges. For without close medical supervision, day-to-day involvement of competent physicians in the delivery of emergency care outside the hospital, and consideration of the influence of time on outcome, an EMS system will prove itself ineffective in reducing morbidity and mortality and might indeed prove detrimental.

It is quite simply a question of control. Without competent physician influence on how medicine is practiced in the streets, there is little hope that EMS can fulfill its mandate. Such control must be far reaching, and must include the ability to decide medical protocols, to determine priorities in the system, to supervise the effectiveness of the system through an adequate program of quality assurance, and to decide where and how money is spent. This control, and not funding, training, or gadgetry, is the greatest challenge facing EMS physicians in the 1980s. Prehospital care is the practice of medicine in the streets, and the role of EMS physicians as patient advocates should be to ensure that such practice is of the highest quality, current, caring, and based on sound science. Concern for this issue has prompted the formation of the National Association of EMS Physicians. The purpose of this organization is the fostering of better prehospital care through education and physician involvement.

It has been shown that a good EMS system can save lives and reduce suffering. It has also been shown that when this delicate medical instrument is not used well, or when it gets rusty, results will fall short of expectations, and patients will be ill served. The challenge of the 1980s for EMS physicians is to prove themselves through proper research and the evaluation of outcome. Otherwise, they will find themselves still shuffling along the dusty road, oil and wine in their packs, kindly seeking to help the victims of thieves, their donkeys trotting along behind them.

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See also pp 414-421.

Physicians, hospitals, and Diagnosis Related Groups (DRGs): Is control the issue?

While physicians and hospital administrators have not always lived together in perfect harmony, open warfare usually has been avoided.[1] Now, however, the fragile truce may be over.

With their practice patterns and incomes increasingly being modified by social, political, and economic changes, physicians are channeling much of their anger toward hospitals. Though many of the reasons for the physicians' frustrations may lie elsewhere, hospitals have become handy scapegoats. Like the proverbial cats, they are there to be kicked. The underlying reasons for the growing discontent can be attributed to several factors over which physicians believe they are losing control. And the result is misplaced anger.

One of the most significant and frequently cited irritants that physicians must deal with today is the dramatic increase in the number of malpractice cases. The physicians' feelings are, perhaps, best captured in a popular bumper sticker: "Support a Lawyer, Send Your Son to Medical School." The situation has reached critical proportions, manifested by large judgments and greatly increased insurance premiums.

Another factor contributing to physicians' frustrations today is the goal of industry, unions, and government to reduce health-care funding for physicians as well as hospitals. Diagnosis Related Groups (DRGs), Health Maintenance Organizations (HMOs), and Preferred Provider Organizations (PPOs) all have a common focus—to reduce expenditures.[2] They also share a common approach—modifying, or rather controlling, physician behavior.

The third factor helping to diminish physicians' sense of control and well-being is the perception by the public that physicians have become less caring and more interested in material goods than in health care. This accusation is rarely directed at the patient's personal physician, but rather toward a general group somewhere "out there."

Nevertheless, the feelings are powerful, and are often personalized by physicians. The reaction is anger, and it spills out in many directions—against trial lawyers and the tort system; against Medicare, which has both frozen and disallowed fees; against the insurers and purchasers who developed these health-care systems; and against any and all critics of physicians' behavior. Of course, it is also directed at hospital administrators, who are not only tangible and accessible, but are regarded as exacerbating all the other problems, especially when they ask staff physicians to alter practice patterns by discharging patients early. The physicians regard these requests as yet another means of eroding their control, increasing their vulnerability to malpractice suits, and alienating patients.

Before the introduction of DRGs, the cost of physicians' comprehensive, compulsive, defensive, or merely extravagant patterns of ordering tests was diluted and absorbed by the reimbursement system. Now, with DRGs, the hospitals, rather than Medicare, have become the insurers, and their survival is being threatened. The hospitals' need to survive in this new milieu and to simultaneously satisfy physicians' needs to provide patients with what is perceived as quality care, greatly limits the options available to today's hospital administrators.

One way to reconcile these differences is to perceive DRGs not as a problem that belongs exclusively to physicians or to hospitals, but, rather, as a problem shared by both and requiring cooperation.[3]

A model that exemplifies this approach can be found in

the pre-paid practice, the HMO, which serves not only as the health-care delivery system, but also as the insurer. Similar to a hospital operating under DRGs, the HMO receives a fixed sum to provide defined health benefits. If it succeeds in doing so at the allocated premium, it remains solvent. If there is an "overrun," due to the cost of physician services, diagnostic procedures, or greater than projected lengths of hospital stay, the HMO sustains the loss, because it has contracted to provide defined services for a predetermined premium. Under the DRG reimbursement system, hospitals are essentially in the same position, except that physician services are not included in the reimbursement. This is an important distinction, for this means that the physicians are not yet at risk. However, physicians must play a role in the hospitals' solution to DRGs, and therein lies the dilemma.

The methods utilized by HMOs to contain costs can also be effective with fee-for-service practitioners, if the physicians can be persuaded that their professional and financial interests are consistent with those of the hospitals. The successful HMO accomplishes this by demonstrating that its needs and interests and those of the physicians, though not identical, are complementary.

The goal is fairly clear: to develop awareness that physicians' as well as hospitals' practice patterns have far reaching financial implications. For example, the cost of cardiac ejection fraction testing does not merely reflect the cost of the procedure; it also includes the additional day of hospitalization, which physicians should remember is paid for by their hospital and not by Medicare. On the other hand, a one-, two-, or even three-day delay in scheduling can make a computerized tomographic scan $600, $1,200 or $1,800 more expensive, without improving the quality of the image or care. Clearly, inappropriate ordering of tests is physician-generated, but delay in carrying them out expeditiously is a dysfunction of the hospital's administration. By understanding the various responsibilities, accepting them, and dealing with them, physicians will experience less loss of control.

A critical key to solving this dilemma is education. The players are entitled to a description of the game, the rules, and the penalties, and a definition of what constitutes winning. Hopefully, this will enhance the players' performance; it is certainly consistent with due process.

Although simply understanding the history and operation of DRGs has proven to have little impact on physician behavior, the educational process is the start. Fee-for-service practitioners, although conscious of the cost implications of diagnostic studies, therapies, and hospital stays, do not perceive them as burdensome to patients, because the costs are passed on to the insurers. These practitioners are the patient advocates, not those of the third-party payers. There is, therefore, little point in stressing that the cost really affects all the participants, including the patient and the physician. However, if it can be demonstrated that the survival of the hospital, as well as its enhanced diagnostic and treatment facilities, optimum staffing patterns, and emergency room functions are in jeopardy, a sense of loyalty could modify the physicians' behavior.

While fee-for-service physicians do not readily associate increased testing and lengths of stay with increased costs—because third party insurers serve as buffers—HMO physicians see increased costs, followed by higher premiums and the HMO's decreased marketability, as closely related phenomena. This is an important distinction between fee-for-service and HMO physicians. The latter are at financial risk and have accepted accountability in exchange for other benefits. They share the fortunes of the HMO, good or bad, and, therefore, do what they can to insure that the HMO and they survive. HMO physicians are more vulnerable to peer pressure and to loss of supplemental income.

These concerns do not exist to the same degree among fee-for-service physicians, who, though they have functioned side by side with administrative staffs, have rarely been faced with survival as an issue. Fee-for-service physicians expect hospitals to run smoothly and to provide prompt, quality laboratory and radiographic services as well as good housekeeping and meals, and, of course, readily available beds. Hospital administrators expect the medical staff to refrain from interfering to any degree in the hospitals' operations and to keep beds filled. With prospective reimbursement, however, hospitals have become more dependent on physicians' cooperation. Extravagant use of procedures and prolonged hospital stays produce hospital deficits. Only if physicians appreciate that their fiscal and professional comfort is related to that of the hospital will they alter their practice patterns.

Measures to preserve hospital revenue without diminishing accessibility and quality of care were begun at a tertiary care medical center in the New York area many months prior to the January 1, 1986 DRG start-up date. While it is still too early to evaluate the efficacy of these measures, it could be useful to examine the procedures used to meet the medical center's goals.

The predictable meetings of administrative departments incorporated useful modifications. For example, procedures in the Medical Records Department, laboratories, and radiology services were analyzed and assessed, with changes initiated when indicated. Also, intensive reviews of continuing care and discharge planning programs generated what were considered productive changes. Moreover, new programs and policies in Management Information Systems and Patient Accounts expedited the paper work.

Although not yet at risk in the new reimbursement system, many of this medical center's staff physicians apparently understood and accepted the importance of their role in keeping the institution viable, thereby protecting their own interests.The physician leadership of the medical staff played an integral part in the educational process, often participating with department chairmen in clarifying the issues and the importance of altering practice patterns.

Computer printouts were distributed to staff physicians with more than 50 admissions in both 1984 and 1985. They showed the lengths of stay for each physician's patients by DRG, compared to the average for all of his or her colleagues. The hospital believed that comparisons among physicians in the same institution were more meaningful than comparisons with the national average, because each hospital has its unique problems. Restricting the comparisons to colleagues thus obviated criticism that long stays were related to delays in operating room schedules, overdue diagnostic test reports, and a host of other

difficulties, because these problems were similar for all the physicians in this hospital.

Accompanying this computerized report was a covering letter which stressed that the data were for information purposes only and were in no way a judgment of performance. (Unless charts were audited, with the severity of illness and a more critical description of demographics included, no evaluation of performance was considered possible.) Short of reviewing charts, each physician was to be the judge of whether his or her patient population or practice patterns were responsible for any gross deviation that might exist.

Using a software "grouper" program, another project, dedicated to optimal coding, demonstrated the importance of complete and accurate documentation. For example, some physicians were surprised to learn that written documentation of existing urinary retention or urinary tract infection on the discharge summary of a prostatectomy patient would result in legitimate additional reimbursement to the hospital. Physicians often do not document these conditions, though they are frequently present. In fact, most physicians had difficulty recalling patients who had not had one or both of these conditions prior to surgery.

The New Tough Times, a newsletter, disseminated information geared to helping physicians understand the background of the new reimbursement system, including details on how to comply with and handle the new regulations.

None of the physician-related activities were conducted without the involvement of physician leaders. Excluding them from the process would have seriously blunted the project's efficacy. The project was simply an exercise in participatory management, which, in the past, had not greatly interested hospital administrators or physicians. The latter, until now, had been quite content to be free of administrative responsibility.

It appears that physicians' willingness to participate and to accept a measure of responsibility can be related to their need to experience a measure of control over the changes taking place around them. Sharing control may be a significant factor in the resolution of problems.[4]

Hospitals have experienced considerable drops in occupancy with the advent of DRGs, the proliferation of ambulatory surgical centers, the rise in mandatory second surgical opinions, and the increasingly active Peer Review Organizations (PROs). A hospital with 60% occupancy is clearly at a disadvantage when it comes to regulating physician behavior, and may be compelled to rely on modest seduction to achieve cooperation. Alternatively, a hospital with 95% occupancy, by virtue of its modern facilities, its prestige, or its location, may demand compliance, effecting a short-term solution, at best. It appears that the more desirable, less discordant, and more lasting approach to achieving cooperation between hospitals and physicians lies in developing an association between the two parties, in which each recognizes the need for the other, each feels like an important contributor, and each feels as great a sense of control over its own destiny as the situation permits. The remedy to the "DRG conflict" may, after all, be found in the quality of the interpersonal relationships developed between hospitals and their physician staffs, and in an understanding that the glue of those relationships is concern, mutual respect, and loyalty.

In spite of this concentrated effort to cope with DRGs, other dramatic shifts in health care may warrant more attention. Recently, Dr Henry Desmarais, Acting Deputy Administrator of the Health Care Financing Administration (HCFA), addressed "options for physician payment reform under the Medicare program," concluding, "It is only through capitation that we can strengthen the competitive forces in our health care system."[5]

If Desmarais's analysis is correct, the conflict resulting from doctors' ordering care and hospitals' bearing the cost may be resolved. But harmony will not be reached through mutual interest. Rather, it will come about through recognition of a common enemy. Physicians and hospitals will become the targets of what has been referred to as "the revolt of the payers." The bulk purchasers of health care—government, unions, and large employers—will control their expenditures by establishing reimbursement schedules (either fee-for-service or capitation) and by overseeing utilization.

HMOs, PPOs, and other managed health care systems will be the middlemen—surrogates for the purchasers and subcontractors to the providers. Those who may be inadequately represented, and this should come as no surprise, will be the patients. "Sweet reasonableness" will not do as their advocate. If self-discipline and regulation do not protect them, we will once again be hearing discussions about national health insurance.

The score is 40–Love, and we are not serving. Time may be running out.

> If I am not for myself, who will be for me?
> And if I am only for myself, what am I?
> And if not now—when?
>
> —Hillel

It is now "when."

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Donald F. Foy

On July 1, Donald F. Foy assumed the position of Executive Vice-President of the Medical Society of the State of New York. Prior to assuming his present post, Mr Foy was the Executive Director of the Indiana State Medical Association, a position he had held for ten years.

Mr Foy graduated from Loyola University of Los Angeles, where he received a BS degree in political science in 1956. He later received an MS degree in education from the University of Southern California and an MPH degree in 1967 from the University of California at Los Angeles, School of Public Health. He was an Airman/2C in the US Air Force in Korea and subsequently served in the US Public Health Service where he was assigned to the Division of Health Standards. While in this position, he coordinated a Medicare personnel qualification study, served as a specialist and senior program analyst, and worked in the Division of Allied Health Manpower.

In January 1971, Mr Foy joined the staff of the American Medical Association (AMA) as Director of the Department of Health Manpower. He later served in the AMA as Director of the Management Services Division. While in this position, he was Secretary to the Board of Trustees' Committee on Insurance and was a member of the staff Task Force on Professional Liability. In 1976 he became Executive Director of the Indiana State Medical Association. Since 1978, Mr Foy has been Secretary-Treasurer of the State Medical Association Presidents (OSMAP) and Secretary-Treasurer of the Forum for Medical Affairs. He is a Captain in the US Air Force (retired), and is a member of the American Society of Association Executives and of the American Association of Medical Society Executives.

Low filling pressure cardiogenic pulmonary edema

A complication of venodilatory therapy

ANTONIS MANOLIS, MD, PHILIP VARRIALE, MD, JOHN NOBILE, MD

ABSTRACT. Hypotension and peripheral hypoperfusion developed in nine patients with acute cardiogenic pulmonary edema during interventional drug therapy consisting of intravenous morphine and furosemide (five patients) and intravenous nitroprusside or nitroglycerin (four patients). Hemodynamic assessment coincident with this complication disclosed an inappropriately low pulmonary wedge pressure and cardiac output. Restoration of an optimal left ventricular filling pressure using volume repletion produced a dramatic reversal of this complication and improved cardiac performance.

In the setting of acute heart failure, drugs capable of potent venodilation may generate a disadvantageous left ventricular preload and may undermine effective treatment. Bedside hemodynamic monitoring permits detection of this complication.

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In recent years, the management of congestive heart failure has expanded to include an array of therapeutic options. In addition to digitalis and diuretics as conventional forms of therapy, these options now include potent vasodilatory and newer inotropic agents that are acknowledged for their beneficial, acute hemodynamic effect on cardiac performance. Given this advantage, however, these agents have also spawned new clinical problems and unforeseen complications.

During the past few years, we have encountered nine patients with acute cardiogenic pulmonary edema, in whom severe hypotension and peripheral hypoperfusion developed at the time of the initiation of treatment. Low left ventricular filling pressure was identified as the cause of the unanticipated complication and was attributed to the venodilatory pharmacologic effects of the therapeutic agents. This treatment-related problem, although alluded to in previous reports, has not been sufficiently appreciated.[1–3]

The purpose of this report is to underscore prompt and accurate recognition of low filling pressure cardiogenic pulmonary edema as a complication of drug therapy and to propose appropriate measures for its reversal.

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PATIENTS AND METHODS

Hemodynamic studies were performed in nine patients who were seen at the emergency room of Cabrini Medical Center with a clinical diagnosis of acute cardiogenic pulmonary edema. This group included five men and four women, aged 57–90 years (mean age, 74 years), who sought medical attention at this institution from July 1983 to May 1985. At the time of admission, all patients had unequivocal clinical signs and symptoms of acute cardiogenic pulmonary edema. These included obvious acute respiratory distress, tachypnea, cyanosis, restlessness, diffuse pulmonary bubbling rales, tachycardia, and S3 gallop. The diagnosis was further supported by characteristic findings on chest films that included cardiomegaly, hilar engorgement, patchy and confluent alveolar infiltrates radiating from the hilus, and upper lung venous dilation.

Five patients had elevated blood pressure and, in all nine patients, blood gas studies demonstrated significant hypoxemia (Po_2 ranging from 30 to 58 mm Hg) and metabolic acidosis (pH ranging from 6.93 to 7.33). Coronary artery disease, as the underlying disease, was identified in six patients. In two of these patients, the disease was associated with either hypertension or aortic stenosis; in two patients, it was identified as hypertensive heart disease; and in one patient, idiopathic cardiomyopathy was the anatomical designation responsible for acute pulmonary edema (Table I).

In patients one to five, designated as group A (Table I), initial treatment in the emergency room consisted of a combination of intravenous furosemide (40–100 mg) and intravenous morphine (3–5 mg).

In patients six to nine,[3] designated as group B, a hemodynamic characterization obtained via right heart catheterization (Swan-Ganz) was derived before therapeutic intervention. The findings were as follows: pulmonary wedge pressure ranged between 25 and 38 mm Hg (mean ± standard deviation, 31.2 ± 5.4) and the cardiac index between 1.8 and 2.2 L/min/m^2 (1.97 ± 0.17). In this group, two patients received intravenous nitroprusside (75 μg/min and 150 μg/min), and two patients received intravenous nitroglycerin (60 μg/min and 150 μg/min).

Early Complications. Group A patients manifested an early complication within one half to three hours after receiving intravenous furosemide and morphine. This clinical problem included severe hypotension with systolic arterial pressure ranging between 60 and 106 mm Hg, associated with an increased pulse rate and signs of peripheral hypoperfusion—cool moist skin, agitation and confusion. Concomitant with this perceived clinical deterioration, a hemodynamic assessment using Swan-Ganz catheterization was obtained. In these five patients, an excessively low pulmonary wedge pressure was noted, ranging between 1 and 11 mm Hg, in association with a low cardiac index ranging between 1.9 and 2.2 L/min/m^2 (Fig 1).

TABLE I. Characteristics of Nine Patients with Low Filling Pressure Cardiogenic Pulmonary Edema

	Clinical profile					Arterial blood gases		Hemodynamic profile		Therapy
Patient	Sex	Age (yr)	Underlying disease	Blood Pressure (mm Hg)	Heart rate (/min)	pH	PO_2 (mm Hg)	Pulmonary wedge pressure (mm Hg)	Cardiac index (L/min/m²)	Drugs administered (intravenous)
Group A										
1	F	82	Coronary artery disease	170/100	124	7.15	35	—	—	Lasix, 100 mg Morphine, 3 mg
2	F	76	Cardiomyopathy	100/70	100	7.34	33	—	—	Lasix, 40 mg Morphine, 4 mg
3	M	90	Coronary artery disease	140/80	108	7.33	58	—	—	Lasix, 40 mg Morphine, 5 mg
4	F	79	Hypertension	250/130	90	7.19	44	—	—	Lasix, 100 mg Morphine, 4 mg
5	M	73	Coronary artery disease	140/100	96	6.93	57	—	—	Lasix, 60 mg Morphine, 5 mg
Group B										
6	M	82	Coronary artery disease	140/80	120	7.21	48	25	2	Nitroglycerin, 25 μg/min
7	F	62	Coronary artery disease Hypertension	230/130	120	7.16	40	30	2.2	Nitroprusside, 75 μg/min
8	M	57	Hypertension	280/160	110	7.05	30	32	1.8	Nitroprusside, 150 μg/min
9	M	67	Coronary artery disease	110/80	130	7.28	53	38	1.9	Nitroglycerin, 60 μg/min

Late Complications. Group B patients demonstrated initial clinical improvement, with a fall in pulmonary wedge pressure and a rise in the cardiac index. This beneficial hemodynamic and clinical response lasted approximately one to two days. In these same patients, clinical deterioration occurred 24 to 48 hours after therapeutic intervention. This complication consisted of hypotension and a hypoperfusion syndrome similar to that described for group A patients. Concomitant with this deterioration, hemodynamic monitoring demonstrated a reduced wedge pressure ranging between 5 and 10 mm Hg (mean, 8 mm Hg) and a reduced cardiac index ranging between 1.6 and 2 L/min/m² (mean, 1.85 L/min/m²) (Fig 1).

Results

The drug therapy given to patients in groups A and B was aimed at elevating the pulmonary wedge pressure. For this purpose, volume expansion with a colloid solution in the form of Plasmanate was given to four patients and 6% hetastarch in 0.9% NaCl was given to five patients. The amount given to each patient ranged between 200 and 1,200 cc (average, 633 cc). The therapy was discontinued when an advantageous filling pressure was achieved. Infusion time ranged between one and a half hours and three hours.

Effects of Volume Expansion. After volume expansion (Fig 1), the augmented pulmonary wedge pressure ranged between 12 and 18 mm Hg (mean, 15.8 mm Hg). This represented a mean increase of pulmonary wedge pressure of 9.6 mm Hg as compared to the average measurement obtained during hypoperfusion. The rise in cardiac index ranged between 2.4 and 3.5 L/min/m² (mean, 2.9 L/min/m²); this represented an increase of 48% as compared to the average measurement taken during hypoperfusion.

A marked clinical improvement was observed concomitant with this hemodynamic response. The patients' blood pressures increased to within a normal range, and their heart rates fell below 100/min.

Discussion

An elevated left ventricular filling pressure (LVFP) and decreased cardiac output are invariably present in untreated acute cardiogenic pulmonary edema.[4] Therapeutic options, including those considered conventional—oxygen, morphine, and diuretics—have recently expanded with the introduction of unloading agents (vasodilators).[5-8]

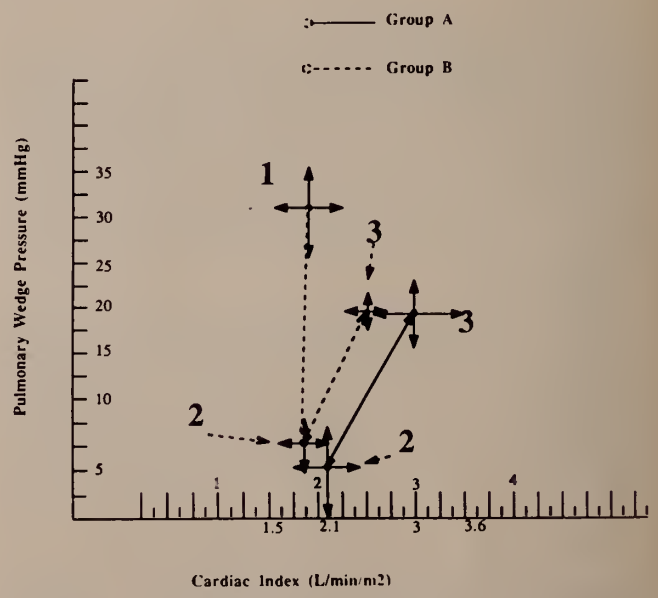

FIGURE 1. Relationship between pulmonary wedge pressure and cardiac index for groups A and B patients, at the time of admission (1), during hypoperfusion (2), and subsequent to volume expansion (3). During hypoperfusion (2) the depressed cardiac index of 2.06 L/min/m² (group A) and 1.85 L/min/m² (group B) was associated with a low filling pressure of 4.8 mm Hg and 8 mm Hg respectively. Cardiac output improved for both groups following restoration of an appropriate filling pressure (3).

Preload, expressed as the left ventricular filling pressure, is considered a major determinant of cardiac performance, and its relationship to stroke volume or cardiac index may be depicted as the left ventricular function curve. The curvilinear relationship noted in normal circumstances is flattened in heart failure, and a higher than normal filling pressure may be required to maintain cardiac output. Conversely, a depressed cardiac output may be further compromised when the LVFP falls below this optimal level (eg, 15–18 mm Hg).[7,9,10]

Hypotension and peripheral hypoperfusion, incident to reduced cardiac output, developed in these nine patients after initiation of therapy and was clearly linked to a disadvantageous LVFP (6.2 ± 4 mm Hg). Restoration of a more advantageous filling pressure (15.8 ± 1.8 mm Hg) using volume repletion promptly and dramatically reversed this complication and established a more satisfactory hemodynamic and clinical state (Fig 1).

Given their well recognized physiologic effect on preload (Table II), it is reasonable to conclude that the pharmacologic agents used for the initial treatment of heart failure were clearly implicated as the cause of an excessively low filling pressure.

Intravenous furosemide, a potent diuretic, is commonly selected as the preferred agent for the rapid relief of pulmonary congestion. It is noteworthy that the drug's anticongestive action is almost immediate and is not related to its diuretic effect.[11-13] A significant increase in venous capacitance that accompanies an early fall of LVFP, often within 15 minutes, has been documented, and this fall in LVFP is only later augmented by diuresis and electrolyte excretion.

Reduced venous return is also an acknowledged property of morphine, based on its physiologic capacity for decreased venous tone and increased splanchnic pooling.[14] The combined effect of furosemide and morphine on preload may be additive and, in some instances, depending on dosage, may account for an excessive fall in pulmonary wedge pressure.

Vasodilators, recognized for their therapeutic usefulness in the management of heart failure, often achieve hemodynamic and clinical improvement by their unloading action.[5] Nitroprusside, a parenteral vasodilator, is considered a balanced (arterial and venous) dilator. In congestive heart failure, impressive reductions of pulmonary wedge pressure—ranging between 30% and 52% of control measurements—have been demonstrated,[5,6,15-19] and a proportionately greater effect on preload has been noted when the filling pressure is initially very high. Nitroglycerin and nitrate esters, also used as therapy for the failing heart,[8,20] have a dominant venodilatory effect and an influence on filling pressure comparable to that of nitroprusside. Low filling pressure and low cardiac output as complications of venodilatory therapy that lead to hypotension and hypoperfusion can be effectively and drastically reversed by simply restoring an optimal filling pressure using volume repletion.

It is well recognized that dosage titration of parenteral vasodilators requires precise hemodynamic assessment, often using a Swan-Ganz catheter. Accurate monitoring will disclose the exact cause of an unanticipated deterioration in cardiac function during treatment. In the specific instance of low filling pressure acute cardiogenic pulmonary edema, induced by venodilatory treatment, this complication may be avoided or, when present, quickly recognized and treated.

TABLE II. Vaso-dilatory Properties of Medications Employed in Nine Patients with Low Filling Pressure Cardiogenic Pulmonary Edema

	Arteriolar dilation	Venodilation	Peak effect
Nitroprusside	++++	++++	1 min (IV)
Nitroglycerin	+	++++	1 min (IV)
Furosemide	0	++ → +++	10–15 min (IV)
Morphine	+	+ → ++	10 min (IV)

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Emergency medical services: Twenty years of growth and development

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Emergency medical services (EMS) in the United States are undergoing major expansion, development, and change. From undergoing a period of "neglect" prior to 1966 to being the recipient of major emphasis by public and private agencies during the 1970s, EMS has experienced progress and improvements, resulting in the development of new systems, new personnel, and a new specialty in medicine. Advances in emergency medical services have occurred as a result of applying a systems approach and by integrating both the hospital and prehospital phases of emergency medical care. New personnel include emergency medical technicians, paramedics, emergency department nurses, and physician specialists in emergency medicine. In September 1979, Emergency Medicine was approved as the 23rd medical specialty, culminating a more than ten-year movement toward the creation of Emergency Medicine as a specialty.

This presentation deals with the development of emergency medical services during this period, the causes for the growth of EMS, and a review of the major accomplishments in emergency medical care.

THE TURNING POINT

In 1966, the National Research Council of the National Academy of Sciences published its landmark paper describing the status of emergency care in the United States. "Accidental Death and Disability: The Neglected Disease of Modern Society," [1] prepared by the Committees on Trauma, Shock, and Anesthesia of the National Research Council, clearly identified the key issues and problems faced by this country in providing emergency care. The council's summary report[2] is worth noting, because it listed factors contributing to the then inadequate US emergency care system:

- The general public is insensitive to the magnitude of the problem of accidental death and injury.
- Millions lack instruction in basic first aid.
- Few are adequately trained in the advanced technique of cardiopulmonary resuscitation, childbirth, or other life-saving measures.
- Local political authorities have neglected their responsibility to provide optimum emergency medical services.
- Research on trauma has not been supported or identified at the National Institutes of Health on a level consistent with its importance as the fourth leading cause of death, and a primary cause of disability.
- The potentials of the US Public Health Service Program in accident prevention and emergency medical services have not been fully exploited.
- Data are lacking on which to determine the number of individuals whose lives are lost through injuries compounded by misguided attempts at rescue and first aid, absence of physicians at the scene of the injury, unsuitable ambulances with inadequate equipment and untrained attendants, lack of traffic control, or the lack of voice communication facilities.
- Helicopter ambulances have not been adapted to civilian peacetime needs.
- Emergency departments of hospitals are overcrowded, some are archaic, and there are no systematic surveys on which to base requirements for space, equipment, or staffing for present, let alone future, needs.
- Fundamental research on shock and trauma is inadequately supported; medical and health-related organizations have failed to join forces to apply knowledge already available to advanced treatment of trauma, or educate the public and inform Congress.

A survey taken in 1965 of 900 US cities reported that less than 23% of these communities had an ordinance regulating the ambulance service; even a smaller percentage required an attendant other than the driver. Training of ambulance operators was minimal with only 72 out of 900 reporting training even at the level of an American Red Cross advanced first-aid course.[3]

The hearse-type vehicles and station wagons generally in use did not have enough room to allow personnel to provide basic cardiopulmonary or other supportive treatment to cardiac, trauma, or other critically ill patients. The vehicles were designed to carry coffins and horizontal loads and not to support a medical team with a sick patient.

Two reports prepared in the mid-1960s dramatically focused national attention on the hazardous conditions of the nation's ambulances.[1,4] In addition to the inadequacy of policies, staff, training, and communication systems, ambulance design was faulty and necessary equipment was absent or inadequate:

- Fifty percent of the ambulance services were run by morticians because they owned the only vehicle capable of carrying patients horizontally;

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- No manufacturer built a vehicle that could be termed an ambulance;
- No vehicle design standards existed;
- Equipment and supplies were incomplete or absent.

Emergency departments themselves were cited as being woefully inadequate. There were more than 7,000 accredited hospitals in 1965, but very few of the hospitals could meet the increased need for emergency services that occurred between 1945 and 1965. The number of emergency department visits increased from 18 million to more than 49 million during the period of 1958–1970.[5] In addition, these emergency departments were staffed by the least experienced personnel, generally interns, with little or no training in the treatment of multiple injuries or medical emergencies. The need for medical leadership was clearly recognized. The American College of Surgeons and the American Academy of Orthopedic Surgeons had published documents during the 1950s and early 1960s in an effort to improve this phase of emergency services; but effective medical leadership was nonexistent, and these efforts were largely ignored.[6-11]

The general public took it for granted that every emergency department could render full care for all injuries and emergencies, but, in reality, not every hospital could afford—or have available—both the equipment and personnel necessary to meet the full scope of medical emergencies. A paper from the National Academy of Sciences recommends categorization of emergency units depending on physical availability, nursing staff, equipment, and training. Four categories were proposed, ranging from facilities that did not have a full-time physician to those facilities that had trained, experienced trauma teams. The latter would house a trauma research unit that would combine patient care with research facilities and would permit investigations into the appropriate therapy and treatment of the seriously injured patient.

Governmental and Private Efforts

Department of Transportation (DOT). The President's Commission on Highway Safety published its final report in 1965, entitled "Health, Medical Care, and Transportation of Injured." This document recommended a national accident response program to reduce deaths and injuries from highway accidents. Its findings complemented and were consistent with the National Academy of Sciences' document described above. Issues, problems, and recommendations of both these documents were used to draft legislation that enabled the Department of Transportation to play the first major federal role in developing a national program for emergency medical services. Public Law 89-564, the Highway Safety Act of 1966, was enacted on September 9, 1966. The Department of Transportation was given legislative and financial authorization to improve emergency medical services. Particular emphasis was placed on the development of a highway safety program and the development of standards and programs for improving ambulance services and prehospital personnel.

As a program that required matching funds from state and local governments as well as private sources, the Highway Safety Act served as a catalyst for millions of dollars to be targeted for the development of emergency services in this country. Since 1968, DOT contributed more than $142 million under Standard II of the act for the development of the EMS system. Between 1967 and 1979, $10 million was spent for more than 50 research funds managed by the National Highway Traffic Safety Administration. Projects fall into three main categories: development, $584,000; demonstrations, $4,919,000; studies/surveys, $5,340,000. This effort resulted in the development of criteria for helicopters, ambulance design, communications manning programs, and plan development.[12-14]

Foundation Support. The Robert Wood Johnson Foundation allocated $15 million in 1974. Forty-four regions received grants of up to $400,000 to develop emergency medical services systems.[15] This was the single largest contribution by a nonprofit foundation for the development of health systems in the United States. The money was used to encourage communities to develop regional systems with emphasis on the foundation's goal of improving access to general medical care.

National Professional Organizations. Many existing professional organizations began to focus on emergency medical problems including clinical, educational, and service components. Established organizations include the following: Committee on Trauma, American College of Surgeons; Committee on Cardiopulmonary Resuscitation, American Heart Association; Committee on Acute Medicine, American Society of Anesthesiologists; Committee on Injuries, American Academy of Orthopedic Surgeons.

Several new organizations were formed that directed their efforts primarily towards improving emergency care and nurturing a new group of health professionals: Commission on Emergency Medical Services of the American Medical Association; Committee on Community Emergency Health Services of the American Hospital Association; American Trauma Society; University Association for Emergency Medical Services; Emergency Nurses Association; Society of Critical Care Medicine; Registry of Emergency Medical Technicians; American College of Emergency Physicians; The National Association of EMS Physicians.

The Emergency Medical Service Systems Act of 1973, Public Law 93-154

By 1973, several major principles were emerging from the demonstrations, projects, and studies completed during the previous few years. A regional systems approach toward emergency medical services was required. Strong federal leadership at the executive branch of government would be necessary, with the Department of Health, Education and Welfare (DHEW) being designated as the lead agency. Hundreds of federal agencies, programs, and laws influenced the various components of emergency medical services. However, there was no coordination or overall direction of program goals. DOT had made major improvements in the prehospital phase, with emphasis on ambulance design criteria, personnel training, and state regulations affecting the prehospital system. Voluntary groups and nonprofit agencies recommended improvements in communication and transportation systems. The federal initiatives to date were limited to five demonstra-

tion projects under DHEW funded in 1968. By 1973, professional, community, local, and state organizations were supporting further involvement at the federal level aimed at achieving major program goals and funding support.

In November 1973, the Emergency Medical Services System Act (Public Law 93-154) was signed into law. It added Title XII to the Public Health Service Act for EMS systems and research grants and contracts, and added to Title VII of the act a new section 776 for EMS training grants. It was subsequently amended in 1976 (Public Law 94-573), 1978 (Public Law 95-626), and again in 1979. The goal of PL 93-154 is to develop a comprehensive emergency medical service system throughout the country, and thereby improve the quality of patient care and reduce morbidity and mortality.

Grant support was made available to communities for developing a comprehensive EMS system. Funds were divided among three sections of the law: Section 1202, for feasibility studies and planning; Section 1203, for the establishment and initial operation of EMS systems; and Section 1204, for expansion and improvement. Fifteen components were authorized for development: manpower; training; communications; transportation; facilities; critical care units; public safety agencies; consumer participation; access to care; patient transfer; coordinated patient record-keeping; public information and education; review and evaluation; disaster plan; mutual aid.

Strategy and Implementation. Since fiscal year 1974, federal officials in DHEW and its successor agency, DHHS, have carried out the mandate of this law guided by several principles that evolved from the earlier experiences of DHEW and private agencies. An effective and comprehensive emergency medical service must have resources sufficient in quality and quantity to meet a variety of demands. The concept of regionalization dictated the establishment of discrete geographic areas with sufficient populations and resources that would enable the region to be self-sufficient.

All states have designated an EMS coordinating agent for statewide EMS efforts. There are 304 EMS regions nationwide.

Progress and Accomplishments

The Emergency Medical Services Act of 1973 and subsequent amendments were enacted in response to public and private pressure to reduce mortality and morbidity among the American people by improving emergency medical services. This was essentially accomplished, and development continues. The focus has been on communication systems, transportation, organization, and system and health personnel. Emergency medical technicians, emergency nurses, and emergency physicians have evolved.

Communications. Prior to the 1970s, there were few, if any, communication systems for emergency care. An estimated 5% of ambulances had voice communication with hospitals, a universal telephone number "911" was not in use, and telephones were not available on US highways and rural roads where most accidents occur. Central dispatch was limited, and studies in the late 1960s documented multiple problems with communication systems, in terms of community resistance, cost, and technology.

DOT funding, established under the Highway Safety Act of 1966, facilitated major steps toward overcoming the communication deficit.

National conferences, seminars, and public awareness programs advocated methods for a universal communications system for EMS. A communications manual published in 1972 provided technical and systems information.[16] In 1973 the "911" universal emergency number was advocated and was promoted as a standard by DOT and the White House Office of Telecommunications. Federal communication Docket #19880 established rules and regulations for EMS communication and set aside radio frequencies for emergency systems. In 1977, DHEW issued guidelines for a communications plan.[17]

The effectiveness of these DOT efforts and those under EMS funding can be estimated by a review of the impact evaluation statements from the 183 EMS regions studied in 1978. Sixty-two percent of the projects reported utilization of the "911" number, covering 18.5% of the country and 34.1% of the population. Central dispatch of ambulances occurred in 40% of the projects, involving more than 60% of ambulances. Medical control of ambulances with physician supervision occurred in 48% of patients being transported.[18]

DOT reports showed that in 1978, 79% of all ambulances in 54 states and territories had two-way voice communication systems.[12]

Transportation. Public Law 89-564, the Highway Safety Act of 1966, was drafted based on the findings of these 1978 DOT reports, and it initiated the major developments achieved during the next 15 years. Under Standard 11, "Emergency Medical Services," states were required, as part of the highway safety program, to meet federal standards for ambulance design, equipment, personnel, training, and communications. DOT developed these standards in conjunction with professional groups such as the National Academy of Science, American College of Surgeons, American Academy of Orthopedic Surgeons, and others.[12]

The 1978 impact study of 183 EMS regions described the status of ambulance services within 151 regions. Of the 13,790 ambulance vehicles in these regions, 60%–65% met federal standards. Eighty-one regions had advanced life support capability, and 72 regions had some type of air ambulance capability. Response time was less than 10 minutes in urban areas and 15 to 30 minutes in rural areas.[18]

Organizations and Systems. A recent survey of EMS in America's 100 most populous cities describes additional changes in emergency medical services.[19] There are 48 million inhabitants in the top 100 cities, ranging from New York with 7,035,000 people to Fort Lauderdale with 152,000. Ninety-one of the cities—accounting for 44,306,000 people—are served by advanced life support systems. Analysis of data collected in this survey shows the breakdown of emergency medical services by ownership and organizational structure (Table I).

Estimates of the number of patients transported were based on state field trip reports, the American Hospital Association's annual tabulations, and guidelines from the American College of Emergency Physicians. Table II contains the 1980 estimates based on this analysis.[19] Using data from the "100 Cities Survey," data collected from

TABLE I. Emergency Medical Services by Ownership and Organization Structure in 100 Cities, USA, 1980[19]

Primary prehospital emergency care provider organization		Base number 100 cities
Fire Department		56%
Cross trained dual personnel	50%	
Civilian personnel	6%	
Third service/public		25%
Third service, municipal	11%	
Third service, county	8%	
Hospital	3%	
Public utility	2%	
Public transportation	1%	
Private		16%
Private ambulance service	15%	
Private ambulance/independent	1%	
Miscellaneous (Police Department, volunteers)		3%
Total		100%

suburban areas, and the above figures on patient encounters, an estimated 52% of the total US population (113,808,904 people) now have access to these potentially life-saving services.[19]

This same survey yielded estimates of the number of ambulance services and their affiliations: 14,425 ambulance services, compared to 37,000 law enforcement agencies and 35,000 fire protection agencies.[20] An analysis of Table III reveals that 48.5% of all ambulance services in the United States are volunteer organizations. This makes the volunteer sector the largest in prehospital care and transportation. These 14,425 services operate 38,947 ambulances, or 2.7 vehicles per service.[19] This compares to 140,000 fire department vehicles, or four per department, and 166,500 police vehicles, or 4.5 vehicles per police agency.

Emergency Medical Technicians

The Department of Transportation funded the development of a training course and textbook for training Emergency Medical Technician-Ambulance (EMT-A) personnel. Published in 1969 by the American Academy of Orthopedic Surgeons, the textbook has become the mainstay of training during the past decade. It was most recently revised in 1981.[21]

In 1969, 200 people took the course—requiring about 81 hours—and were among the first group of formally trained ambulance personnel. The job description was further defined and officially recognized by the Department

TABLE II. Number of Emergency Patients Treated and/or Transported, 1980 Estimates[19]

Type of care	Number of patients
EMS personnel provided first aid but no transportation	2,450,000
Patients transported by ambulance vehicles	7,707,619
Patients transported by police vehicles that are not ambulances	1,479,240
Total number of patients treated and/or transported by EMS personnel in 1980	11,636,859

TABLE III. Ambulance Services by Affiliation, USA, 1982[20]

Volunteer services related to a fire rescue department	4,950 (29.5%)
Volunteer services that are independent of any other organization	2,550 (19%)
Fire services with paid career personnel	2,122 (16%)
Health Department and hospital-based services with paid career personnel	410 (3%)
Police services with paid career personnel	463 (3.5%)
Governmental ("Third Service") services on a city, county, or regional basis with paid career personnel	940 (7%)
Private for-profit services with paid career personnel	2,420 (18%)
Others (military, industrial, etc)	570 (4%)

of Labor as an occupational specialty in 1972. Emergency Medical Technician-Ambulance (EMT-A) and Emergency Medical Technician-Paramedic (EMT-P) became the mainstays of prehospital care.

The EMT-A is trained to provide basic emergency care at the scene and during transport to a hospital emergency service. Skills include basic cardiopulmonary resuscitation, control of bleeding, extrication, and transport of the injured patient. The educational requirements in a standard approved program consist of approximately 80 to 100 hours of didactic lectures, practical experience, and hospital observation. Graduates of the program must work six months prior to taking a certifying examination administered by the National Registry of Emergency Technicians. Founded in 1970, the registry has standardized the examination and certifying process for EMT-A personnel. Continuing medical education is a requirement for maintaining registration and certification.

A more advanced, sophisticated EMT emerged during the 1970s. The Emergency Medical Technician-Paramedic (EMT-P) provides advanced life support to patients at the site of the emergency. The EMT-P curriculum covers 600 to 1,000 hours of training, including didactic material on all emergency conditions, clinical skills, and hospital experience. Clinical skills include defibrillation, intubation, venipuncture, and the use of drugs based on interpretations of the victim's clinical signs, electrocardiogram, and history of illness. Telemetry, written protocols, and voice contact to an emergency physician provide medical backup and control.[22]

Emergency Medical Technician-Intermediate (EMT-I) is the most recent category of EMTs. The level of training is in between EMT-A and EMT-P, and these individuals are able to start intravenous therapy, stabilize trauma patients, and use more advanced techniques in establishing an airway and transporting patients.

National Board Certification for EMT-I was approved in June 1980 by the National Registry of Emergency Medical Technicians. Seven organizations (the American College of Emergency Physicians, the American College of Surgeons, the American Medical Association, the American Psychiatric Association, the American Society of Anesthesiologists, the National Association of Medical Technicians, and the National Registry of Emergency Medical Technicians) have jointly agreed to review curriculum, registration, and certifying requirements.

Throughout the following decade, there was rapid growth and expansion in the number of trained and licensed prehospital personnel, although it is difficult to obtain exact numbers. A nationwide survey taken in 1980, summarized in Table IV, shows the number of EMTs and paramedics licensed and certified in each state.[23]

In the 1970s, when 60% of EMT-As and EMT-Ps worked as volunteers, the economic value of this voluntary service was estimated to be $243 million. In 1980, based on 485,000 personnel with higher salaries, this figure exceeded $500 million.[24]

In a 15-year period, the nation has moved from having virtually untrained personnel on its ambulances to having a cadre of more than 485,000 trained medical professionals, both paid and volunteer, providing emergency care in the prehospital system. The National Association of Emergency Medical Technicians projects that by the 1990s, most ambulances will be staffed by EMT-Ps and first responders (police, firefighters, etc) trained as EMT-As.

Emergency Department Nurses. In many hospital emergency departments throughout the country, especially in rural areas where physicians are not present at all times, the emergency department nurse is the first provider of emergency care. In urban and teaching hospitals, where poorly supervised, inexperienced house officers are often on duty, emergency department nurses represent the most experienced personnel during the first crucial minutes of treatment. Nurses also provide medical backup via voice communication and telemetry to the thousands of EMTs who provide care at the site of the emergency.

Until the early 1960s, there were no formal training programs or certification programs for the specialized skills and knowledge possessed by some emergency department nurses, but required by all. Few people were even aware of the profession, and there were no associations to represent its members.

The American College of Surgeons sponsored some programs for nurses in the mid-1960s, but it was not until the beginning of the EMS development in 1966 that meaningful changes occurred in the nursing profession.

In 1968, in Buffalo and Rochester, New York, several emergency department nurses organized themselves professionally around emergency nursing. In 1970, the Emergency Department Nurses Association (EDNA) was nationally incorporated. Now called the Emergency Nurses Association (ENA), its objectives were to define and implement standards of quality emergency nursing care. They have taken a leadership position in representing emergency nursing in government, emergency health councils, organized nursing, and in teaching centers.

During the past ten years, ENA has developed a core curriculum for emergency nursing, organized seminars and courses, and established emergency nursing as a specialty within the American Nurses Association (ANA). ENA has also published "Standards of Emergency Nursing Practice" through the ANA, initiated the *Journal of Emergency Nursing* (JEN), and established a certifying examination for emergency nursing.[25] In July 1980, the first certification examinations were held; those who successfully passed this written examination were recognized as Certified Emergency Nurses (CEN).

Currently, there are 12,000 nurses in the more than 250 local ENA chapters throughout the country. ENA estimates that there are more than 70,000 nurses working in emergency departments and handling more than 77 million patient-visits.

Emergency Medicine Physicians. In 1966, the National Academy of Sciences' National Research Council publication stated, "No longer can responsibility be assigned to the least experienced member of the medical staff, or solely to specialists who, by the nature of their training and experience, cannot render adequate care without the support of other staff members." [26] This far-reaching document identified the importance of having physician leadership and specialty training in emergency medicine. During the 1950s and 1960s, increasing demands for emergency care were placed on hospitals throughout this country as a result of increasing specialization, declining numbers of general practitioners, increasing medical technology based within the hospital, greater expectations by the public, and increasing third party insurance support for emergency care. The number of emergency department visits was also increasing. It is estimated that 80% of visits to emergency departments were for less than life-threatening care, or for care that would have previously been given in a physician's office; 15% were for emergencies requiring immediate attention; and 5% were for treatment of critically ill patients. The specialty of emergency medicine evolved to deal with the 5%, the critically ill patients, and developed the academic discipline and scientific rigor necessary to define the knowledge and clinical skills required to meet the needs of this patient population. Increased medical knowledge and advanced technology gave greater hope for saving the lives of critically ill patients, and the public demanded improved medical care to reflect these advances.

In 1968, the American College of Emergency Physicians was formed and has grown to more than 11,700 members in 1985.

In 1970, the first emergency medicine residency was established at the University of Cincinnati. The first Department of Emergency Medicine in a medical school was formed in 1970 at the University of Southern California in Los Angeles. At the same time, the University Association for Emergency Medical Services was founded by directors of medical school emergency departments. Between 1972 and July 1984, more than 1,500 residents completed training programs in more than 65 emergency medicine residencies throughout the country.[27-29] The first major step toward certification as a specialty occurred in 1973, when the American Medical Association authorized formation of a provisional Section of Emergency Medicine. In 1974, the Committee on Board Establishment was appointed, and a liaison Residency Endorsement Committee was formed. During subsequent years, standards for emergen-

TABLE IV. Emergency Medical Technicians, 1980[23]

Type	Number
Basic life support, EMTs (EMT-A)	430,777
"Intermediate" EMTs (EMT-I)	23,087
Advanced life support, paramedics (EMT-P)	32,074
Total	485,938

cy medicine programs were adopted, certification examinations were prepared, and the American Board of Emergency Medicine was formed.

A major impetus toward further expansion of the residency program in emergency medicine occurred with the formation of the American board in 1976. Prior to that time, there was hesitancy in creating residencies and programs that would not lead to board certification. Major financial support became available in 1976, when the amendments to the Emergency Medical Services Act of 1973 allocated significant amounts of money for the training of emergency physicians. By 1985, 2,852 physicians had been certified as diplomates.

In the mid-1970s, continuing medical education, or mid-career training, formed an important part of the effort in the production of emergency medicine specialists. Most physicians engaged in emergency medicine on a full-time basis had been trained through clinical practice and experience. It was important, therefore, to provide a continuing medical education program in addition to the residency programs during this period. With approximately 15,000 physicians currently engaged in full-time emergency medicine, it is obvious that the 1,500 to 1,800 graduates of residency programs in emergency medicine can fill only a small proportion of available jobs. Consequently, most emergency departments in this country are staffed and will continue to be staffed by physicians trained in a variety of disciplines, who have developed expertise in emergency medicine through experience and continuing medical education programs.

In 1985, the residency programs were either two years or three years in duration. The 28 two-year programs, involving 409 residents, required the completion of at least one year of an approved residency program. Most programs now accept residents with more than one year of post-graduate training. The 37 other programs, with 825 residents in training in 1984, had a three-year program of post-graduate study. By 1987, all emergency residency programs will require three years of training and will be under the direction of physicians certified by the American Board of Emergency Medicine.

The emergency medicine physician is now recognized as a formal member of the medical specialty community. Such a physician is defined by the Council on Medical Education of the AMA as one trained to engage in (1) the immediate and initial recognition, evaluation, care, and disposition of patients in response to acute illness and injury; (2) the administration, research, and teaching of all aspects of emergency medical care; (3) the direction of the patient to sources of follow-up care in or out of the hospital as they require; (4) the provision, when requested, of emergency but not continuing care to in-hospital patients; (5) the management of the emergency medical system for the provision of prehospital emergency care.

Emergency medicine physicians have placed increasing emphasis on prehospital emergency care during the past decade. With the expanding technology base and increased training for EMTs, medical leadership and control are of greater importance for quality care and continuing education. To support these goals, the National Association of EMS Physicians was formed in 1984 as a scientifically based, service-oriented organization for the improvement of the emergency medical services system. Physicians with interest and involvement in the prehospital system of emergency medical services have joined to achieve mutual support, to exchange ideas and knowledge, and to participate in research for the improvement of prehospital care.

The New Federalism

Under the new federalism policy of the Reagan administration, categorical funding for EMS had been phased out beginning in fiscal year 1982. Under the new block grant approach to funding emergency medical services, states will have the authority to decide how much money is spent for supporting EMS development. The new Preventive Health and Health Services Block Grant program will support a total of eight programs, including EMS, Health Incentive Grants, Hypertension Control, Rodent Control, School-Based Fluoridation, Health Education/Risk Reduction, Home Health, and Rape Crisis Centers. Since only state governments can apply for these grants, local governments and nonprofit organizations will have no direct access to previously available funds. The organizations will have to lobby and compete for funds available to all eight programs. Governors will have the authority to decide how the funds are allocated among the various programs. This change in funding and regulation will have a major, but still unknown, effect on further development of emergency medical services in this country. One immediate effect has been the phasing out of the division of Emergency Medical Services of DHHS. All EMS activity is conducted by personnel at the Centers for Disease Control in Atlanta, which will administer the Preventive Health and Health Services Block Grant program.

The impact of these changes on continued national growth of EMS and the achievement of goals established during the past ten years is unknown, although an absence of national funding and of a national focus for leadership may result in a slowing, if not a reversal, of the progress achieved since 1966.

System Components and Design. The nation moved toward the development of a network of emergency medical service systems based on the best judgment of system developers during the late 1960s. Untested concepts of prehospital and hospital phases formed the basis for system design, funding guidelines, program development, and EMS implementation. These same elements could also dictate emergency medical services operations for the next decade and beyond. The 1978 National Association of Sciences' National Research Council report urges a "review" of recent efforts avoiding "uncritical allegiance to our first cuts at EMS systems design." However, there exist deficiencies in the present evaluation systems and assessment programs within EMS systems. Research on emergency medical services is just underway and may be able to answer some questions, but long-term issues in system design—the various elements and interrelationships of the system—require several more years of study.

Basic questions concerning the three elements of EMS systems need to be answered. First, the people involved—patients, health care providers, and support personnel—have a variety of standards, training programs, professional allegiances, and needs. Who does what? How are

they trained? Who supervises? Who pays? Who has overall responsibility? Who should be treated? EMS has directed its efforts at reducing disease and disability among the critically ill and injured, yet 95% of the patients treated by emergency medical services fall outside this main goal of EMS. What is the responsibility of EMS to this large majority of more than 77 million patient-visits annually? How will EMS develop, operate, and finance itself when the need is for acute emergency care for 5% of patients, but the demand is for primary and urgent care for the other 95%?

Technology, as a second element of EMS, includes facilities, communication systems, transportation components, and clinical equipment. These subsystems will develop only as system goals are clearly defined, financing is secured, and new methods and procedures evolve. Greater emphasis on high technology to respond to and treat the patient with serious injuries is needed.

A knowledge base that is expanding at every level of the prehospital and hospital system is the third element of the EMS system. Evaluation, modification, integration, and feedback into the system will influence every phase of emergency care. Major efforts are needed to operate a more expensive system with diminishing resources and greater expectations.

Freestanding/Urgent Care Movement. The rapid growth of EMS utilization occurred in part as a response to the need for emergency and urgent care that was not always available in the specialty-oriented medical care system. In the 1980s, a surplus of physicians, changing governmental regulations, restructuring of the financing and organization of public and private insurance systems, and the rapid emergence of the corporate health care system will continue to alter the course of EMS and emergency medicine. Health maintenance organizations, individual practice associations, preferred provider organizations, and urgent care centers, freestanding ambulatory care centers, and national multi-chain hospital-health care systems are revolutionizing the delivery of medicine in the United States and will profoundly alter the organization and delivery of emergency medicine. The total volume of patients treated in emergency departments will decrease, with a greater proportion of patients being true emergencies. Emergency medicine will increasingly treat sicker patients while less sick patients will seek treatment from the newer and less expensive models of health care. More emergency treatment at a greater cost will have serious financial implications for EMS as it is currently structured. Each emergency patient will require more intensive care at a greater expense in an environment of diminishing resources, as less sick (and less costly to treat) patients leave the emergency medical system. Emergency medicine as a clinical discipline will become more focused on the care and treatment of emergencies, narrowing its discipline, but developing emergency medicine more as a clinical specialty.

It was new knowledge in medical science, such as understanding the pathophysiology of cardiac arrest, that enabled life-saving prehospital components such as portable defibrillation and paramedic personnel to be developed and implemented. As the knowledge base broadens, new techniques and procedures, coupled with changes in the organization and delivery of emergency care, will profoundly alter EMS systems throughout the coming decade.

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A critique of fashion in medical education: Some thoughts on the GPEP report*

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INTRODUCTION

Fashion
though folly's child
and the guide of fools,
rules even the wisest
and in learning rules.
—George Crabbe, 1754–1832.

These lines by Crabbe, the East Anglian poet/surgeon/cleric, written about 200 years ago, express well how fashion can dominate the thinking of even the wisest people and is paramount in educational matters. However, though it is easy to complain about the influence of fashion on education, it's not so easy to do much about it in practice. In something as complicated as medical education, where it is virtually impossible to prove or disprove a hypothesis with certainty, arguments may do little but illustrate the prejudices of those taking part. This may explain the reticence of the wiser among us in not adding to the noise levels in such debates. Their most eloquent comment may be their silence. Perhaps I will grow wiser one day and keep my mouth shut but I have been so disturbed and angered by the cynicism and the damage to academic standards and morale that often follow the introduction of half-baked educational systems into our medical schools that I am grateful for being allowed to air some of my prejudices on the subject. I know virtually nothing about educational theory; my thoughts and feelings on medical education[1] come from some 40 years of teaching and being taught in universities in different parts of the world.

In my lifetime I have seen so many fashionable theories wither in the light of experience that my faith in theories as a guide to truth is slim. Experience has shown that most simple theories, whether they deal with economics, politics, education, or whatever, no matter how logical, fashionable, or attractive they sound at the time, usually do not work well when tried out in real life situations. If this means that we must muddle through with pragmatism and what I like to think is common sense, so be it.

Nothing beats experience for evaluating theories. My father was a clergyman. When he was a young minister he gave a talk which was popular at meetings of young mothers in his parishes. He called it, "The ten cardinal points for bringing up children." Then he married and had four normal, healthy children, of which I was the third. The ten points soon fell to seven. When it reached three he abandoned the talk. A generation later, the enlightened theories of Dr Spock provided my wife and me with the up-to-date, modern model we hoped would result in problem-free, happy, and fulfilled children. Now that our children have grown up, I wonder, could this be where we went wrong?

When I was young I was an expert on America. I had watched so many American movies that I felt entitled to pontificate on all things American. In 1960, however, the Harkness Foundation gave me a fellowship to work and travel here. A condition of the fellowship was that, in addition to spending a year or so working in a university, I should spend several months not visiting universities, but exploring the country, meeting people and just going wherever I wished. They provided me with a rented car to do it. Though this seemed self-indulgent and rather offended my work ethic at the time, the four months spent with my wife and baby daughter touring America and meeting Americans were amongst the most memorable and instructive in my life. Never again could I generalize about the characteristics of this great conglomerate of nations, attitudes, life-styles, terrains, and climates. America (and medical education for that matter) does not lend itself to such over-simplifications. The only common thread throughout our journey was the great kindness and hospitality shown to us in all parts of the country.

As an eager young academic, I knew exactly what was wrong with medical education. When I was made chairman of my department I had an early opportunity to correct matters by trying out the newer educational theories on our students which for some strange reason my predecessors had seemingly ignored. To my great disappointment, their implementation often made little difference to the students' happiness or level of achievement, but

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caused them some anxiety and the department considerable extra work and expense. We tried to salvage the best of each new system and graft it onto the old, but mostly it might have been better to concentrate on improving the old system and avoid the disruption that the change in curriculum caused.

It is against this background of lost innocence that I react so negatively to people who complain stridently that traditional medical education is virtually useless, if not harmful, and that if we would only implement the latest new educational theories, it would make it all better. Especially so when it is said in a pompous way with near evangelical zeal on equivocal evidence. Life just isn't as simple as that. I go along with Malcolm Frazer, the ex-prime minister of Australia, who said, "Life wasn't meant to be easy." I hope I will not be thought too complacent for my opinion that the traditional medical curriculum provides one of the most interesting and absorbing courses available in a university. It is not perfect nor would I expect it ever to be so. Nevertheless, I would treat it with respect and not tamper with it lightly since its evolution has drawn on some of the best minds and highest ideals in human history. Some of my early and arrogant efforts to improve our own curriculum were as counter-productive and vandalistic as my effort to improve the appearance of a Victorian brass bed by sawing off its elegant but extravagant superstructure. I am not sorry that the inertia in most medical schools protects them from the worst excesses of educational vandals; that degree of protection is needed today more than ever.

Of course I would not want to prevent change and could not prevent it even if I did. New people and new ideas will always keep our curriculum on the move and it has to adapt to changing times and conditions. That is why it is as good as it is. But I would worry if the rate of change were so great that there was not the time to evaluate the merit or otherwise of the changes introduced or if it resulted in irretrievable loss of some of our traditional strengths.

Perhaps then you will bear with me if I discuss some of the recommendations in the GPEP report, also known as *Physicians for the Twenty-First Century*,[2] since I feel they incorporate some of the fashion of our time. It would be surprising of course if they did not. Though spelt out at some length in the report, they can be summarized briefly. In general they deal with matters of emphasis rather than matters of absolutes. On student selection, it is recommended that medical students should have a broader educational and social background and be selected on personal characteristics rather than just academic performance. On curriculum content, it is recommended that emphasis should be put on principles rather than facts, attitudes and skills as much as knowledge, the medicine of the future as much as the medicine of the past, and the medicine of the community as much as the medicine of the specialist hospital. On curriculum organization, the report recommends that medical education should be faculty- rather than department-based, integrated rather than subject-based, and active rather than passive. With regard to student assessment, it recommends that evaluation should be subjective rather than objective and continuous rather than periodic. It also recommends drawing up clear educational objectives, fostering literacy, and, perhaps predictably, spending more public money on medical education.

Now these sound quite logical and, when younger, I might have accepted them more easily. However, now that I am older I have reservations about them as panaceas for medical education. Just because a thing sounds logical does not mean it will work. Indeed I worry that revolutionary adoption of some of the ideas in an extreme form might weaken the morale and traditional strengths of our schools.

Student Selection

Selection from a Broader Educational and Social Base. It is fashionable to suggest that the medical students we now select have not a sufficient breadth of education. I would be surprised if they ever had! However, to overcome this the report suggests that premedical education should cover not just the natural sciences but the social sciences and the humanities as well. Off the cuff, I suspect that most of us would side with the angels and plump for a broad rather than a narrow education. But on reflection it is not that simple. A study in the breadth suggested could make exposure to each area so superficial that its educational value would be worthless. To produce a good musician, you do not attempt to teach him every instrument. Similarly, you will not produce a good scholar just by exposing him to a little of everything.

I understand the thinking behind the recommendation, however. There is worry that the college efforts of intending medical students are geared excessively to excelling in physics, chemistry and biology to the exclusion of other subjects. Personally, I do not worry too much about that. The best way to learn about learning is to study in depth and it is not impossible to teach the liberal arts through the sciences. Biology, for example, has a history, a geography, a literature, many languages, a mathematics, and a philosophy—not to mention social and ethical implications. There is no reason why a good biologist need be narrow intellectually. For educating the mind, the rapport built between teacher and student may be more important than the subject taught. Exposure to many teachers in short courses covering most of the disciplines taught within a university is no guarantee of a good education if no teacher has time to make much impact.

In advising medical schools not to make entrance requirements too restrictive, the report questions whether medical students need a scientific background to benefit from the course. Many newer schools believe they do not, and may be correct provided the students are bright and motivated. However, I suspect that lack of a science vocabulary must be a handicap for the average student in coping with the average medical course and I advise intending medical students accordingly.

It is popular to argue that students from disadvantaged minority groups should be selected to provide an appropriate mix of medical manpower and to correct social inequalities. The report puts it this way: "Continuing effort is needed to increase the opportunities for under-represented minority students to be prepared for medicine in college and matriculated in medical school." I accept that, but feel that medical schools should not compromise their standards, courses, or procedures to do so. I see medical

schools as places providing medical education of an acceptable standard to all students qualified to benefit from it. I do not see them as instruments for social engineering and my experience suggests that those who do pay heavily for it in educational and human terms.

Selection on Personal as Much as on Academic Qualities. There is a theory that the medical students we select may be too single-minded and too clever to be good doctors and that they do not possess the human qualities and independent learning skills that future doctors will require. My trouble here is my uncertainty about identifying, let alone measuring, the personal characteristics required to be a good doctor. Like everyone else I have my prejudices on what they are but, unless I've known someone for years, I can't be certain they possess them. Even if a psychologist assures me that they do, how can I be certain they will retain them in later life? Personal characteristics are easily simulated. I have been saddened by the mental dishonesty adopted by some candidates as they simulate the attitudes they believe are needed for selection. Inwardly I sometimes cringe when I read those awful essays written by otherwise bright and honest students on why they want to become a doctor. How they had this sudden call as a child to heal the sick and splinted their teddy bears' broken legs. Any system which encourages pretence and mental dishonesty is a poor screen for medicine. I am happier to base selection on objective measures of academic performance. I do not believe there is an inverse relationship between academic skill and humane values. If students do well academically, they must be reasonably bright, reasonably determined, and have reasonable mental and physical health. Can we ask for more? Within the diversity permitted by such objective selection should be most of the qualities that doctors might need in the future.

What worries me even more is the tendency of some of the newer medical schools to recruit staff on the basis of their beliefs and personal characteristics rather than their academic performance. If it is decided to start a new medical school with a particular new philosophy which emphasizes certain personal characteristics, a dean will be found who espouses that philosophy. To prevent the philosophy being subverted, foundation staff are recruited who share or pretend to share those beliefs. An emotional commitment to the belief or philosophy then becomes more important than academic merit when appointments are made. Anyone who criticizes the school credo risks being branded a dangerous heretic or disloyal to the pack. To some extent it's like joining a monastery; one must subscribe to the institutional beliefs to belong. The only real way to question the belief is to resign. I would prefer to work in an institution which will tolerate all varieties of belief and where the only credentials for membership are academic ability and integrity.

Curriculum Content

Emphasis on Principles Rather Than Facts. There is a widespread belief that students spend too much time memorizing facts and that we should reduce scheduled teaching time and the amount of material we expect them to learn. Superficially this is attractive but it worries me for the following reason. I do not think we can understand anything well unless we first take the trouble to immerse ourselves in the facts. Initially, they may seem confusing and disconnected and the subject as a whole may not make sense. Though this is a depressing phase, it is important to learn to press on. If we keep grinding on the pertinent facts drop into place eventually, and the subject as a whole begins to hang together. Concepts emerge. It is a very rewarding and exciting intellectual experience, when, as we say, the penny drops. The length of the latent period between beginning to study a subject and beginning to understand it varies, but in my experience is rarely less than six months. I have tried repeatedly to discover ways of helping students contract or even bypass this latent period; it would so accelerate their education. But I have never been successful. To know a subject, it seems one must first put the facts that underly it into one's head. Using other stores such as floppy discs or library files is no substitute for mental assimilation. And, of course, our heads, especially when they are young, are superb at this, considering the vast amount of new information poured into them every day. What's wrong with memorizing material? We all do it. When examining a patient one should go through an orderly series of drill-like procedures which have been memorized with precision; if one is to be thorough (let alone make a diagnosis), one shouldn't work out the conduct of each physical examination by going back to first principles each time. People say, why memorize facts when one can look them up in a text book or on a video display screen? That is as foolish as saying, why memorize words when they can be looked up in a dictionary? It would be virtually impossible to think or speak if one had to look up every word. Similarly, one can do little in medicine (or anything else for that matter) without a large store of working information in one's brain.

Facts are the only constant reality (though some are more useful than others). Concepts and principles are necessary but they are merely theories to relate a set of facts and are usually ephemeral. Though concepts may seem more exciting than facts, they are no stronger than their factual basis. Take the analogy of the results and discussion sections in a scientific paper. The results section should give the unadorned findings or facts in a disciplined way that should be as true in 100 years' time as it is today. In the discussion section one can hypothesize and elaborate concepts to relate the facts to the heart's content. But, one can and must abandon these concepts when new facts emerge which don't fit. A person whose knowledge is of concepts only lacks the data base from which to question the concepts and, if necessary, develop new ones. David Lagunoff,[3] in a recent letter to the *Journal of Medical Education*, could not have put it better. He wrote:

> Medical students need facts; they need a well developed medical vocabulary and an orderly conceptual framework to create the intellectual context in which reasoning and problem solving become possible. The most astute reasoning is quite useless if it is not carried out in the context of facts.

The Information Explosion. It's fashionable to talk of the "information explosion," which suggests that knowledge and the amount we require our students to memorize is increasing exponentially. This sounds reasonable but it

is not quite like that. I had a great-great-uncle who was one of the first students at our medical school in Belfast about 130 years ago. He was awarded a book prize in physiology on the results of a first year examination in chemistry in 1858. It is a splendid, heavy, leather-bound book which I admired greatly as a child. I can remember thinking how clever doctors must be to know so much. Later, after I read physiology, I began to wonder how so much text could be written at a time when so little was known about physiology. Would, for example, this great tome say nothing about the adrenal cortex on the grounds that nothing of its function was known? Not so—the section on the adrenals was longer than in most modern student texts; it described in detail the structure, blood supply, nerve supply, comparative embryology, and comparative anatomy, hypothesized about this and that, and built up the concept that it might add "nutrients" to the blood. The number of facts to be memorized by the student then was as great as if not greater than it is now; the difference today is that a more pertinent set of facts is presented to the student to allow him to see the present-day concept. In another 130 years I suspect that we won't present the student with more facts about the adrenals, merely more relevant facts to give him the concept of the gland that is fashionable then. This brings us again to the crucial importance of good teaching. From the countless facts available of varying relevance, a teacher must guide students towards those which permit the formation of concepts and if necessary their modification in the light of new knowledge. The teacher does not do the students' work for them, merely points them with the appropriate facts in the right direction.

Information Technology. In all branches of learning today, and medicine is no exception, it is fashionable to argue for better "IT," ie, "information technology," to deal with the "information explosion," and that students should have instruction in its use. To me, there is little fundamental difference between storing information on floppy disks, notebooks, or card indexes and I would give training in the use of computers no more or no less emphasis than I would give to training in keeping good records or in the use of libraries. All seem useful technologies that can facilitate our work. The important thing, it seems to me, is to limit the time wasted by students learning ephemeral skills. I find that as soon as I learn one way of communicating with a computer, they change the language (if not the computer). At one time, people convinced me I should learn the electronics on which medical technology depended. So I spent many happy but rather useless hours constructing a radio from resistors, capacitors, etc. But I was weak on electronics; my radio crackled quite a lot (perhaps because of cold solder joints), and soon my fledgling skills were made obsolete by the introduction of printed circuits. I suspect that doctors should not divert too much time to rediscovering the electronic or computer wheel but should use electronic and computer experts to provide the services they need.

Emphasis on Acquiring Attitudes and Skills as Much as Knowledge. The theory here is that having the proper attitudes, values, and learning skills may be more important than knowledge to doctors of the future and should be stressed accordingly. What about teaching attitudes? Attitudes are important but are difficult to teach systematically without evoking cynicism. You may know of the disadvantaged boy who, when asked to write an essay on police, wrote, "Police is bastards." His teacher, worried by this negative social attitude, took him to a kindly police sergeant who explained at length the social role of the police in protecting the weak, helping the young, and so on. In his next essay on police, the boy's teacher was depressed to see little improvement; all he had written was "Police is cunning bastards." I suppose the only way to teach attitudes and values is by example. Medical students are as perceptive as the youth at the police station, and if they detect a difference between what people say and what they do regarding attitudes and values, they become cynical and their cynicism is justified. It comes back to the crucial factor in education, the quality of the teachers. If the attitudes and values they exhibit through their work are what we would wish, we do not need formal teaching to inculcate them.

Can we teach skills? We can teach people how to do things. I'm not sure we have time to make medical students very skillful at anything. For me personally, skill only comes when I've done the same thing over and over and over again until I'm almost sick of it. A person can be taught to row in an afternoon; it takes years to make an oarsman. So I don't worry much if medical students leave me with only rudimentary skills. They have their whole professional lives to perfect the skills I would like them to have if they are to practice on me in my old age.

It might be good educational practice to teach each student to develop one skill to a high level. This might show that nothing is very easy and that to do anything really well needs hours and hours of practice. Learning this lesson could be important for people whose appreciation of skill may determine what they do, or more importantly don't do, to their patients.

Emphasis on Teaching the Medicine of the Future Rather Than the Medicine of the Past. The theory underlying this recommendation in the report is that since our students must work in the future, there in little point in teaching them the medicine of the past. It is hard to object to this since students who work in the future will find that the incidence of disease and the way it is treated change continually. It raises the important issue, pertinent to all education, of how to train people for work in the future. It is very hard to teach a satisfying course on material where we know virtually nothing. The future falls into this category and it is difficult to teach about it in a meaningful way. I suspect the only useful way to help people cope with the future is to illuminate the past. The past is all we can speak about with authority. If, by doing this, we can show that medical knowledge was seldom static but kept evolving as new techniques gave new opportunities, that problems arose continually and were often overcome, that new ideas kept bubbling up but virtually all proved useless, we can explain where we are today and how we got here. Then we can leave it to the young themselves to carry medicine forward. If they watch us adapt to today's situations and uncertainties, when we fail as well as when we succeed, and see how we draw on lessons learnt from the past, they will learn the tricks and attitudes needed to deal with the unknowns of the future. Teaching through research is par-

ticularly useful here since it gives insight into the thinking needed to solve problems. Here is another reason, if one were necessary, for having the best possible teachers—people for whom solving problems through research and adapting to new situations is second nature; whose attitudes will be as appropriate for work in the future as they were in the past, with a feeling for excellence, hard work, common sense, clear thinking, and above all, intellectual honesty. If such teachers can by their example pass on to their students the ability to think with honesty and simplicity, we needn't worry too much for the future.

It is often said that the medicine of the future will have more to do with health education and preventing disease than with curing disease and that our courses should stress this. This is not a new idea and most of us could support it. I wonder why courses in health education and the prevention of disease are not more successful and popular? Perhaps they don't fit so easily into the Hippocratic tradition of a one-to-one relationship between doctor and patient. I don't see overt resistance in medical schools to teaching health education; I suspect it is just a difficult course to teach well.

Emphasis on Teaching Community Medicine as Much as Hospital Medicine. Since most encounters between doctors and patients do not result in attendance at hospital, the report advises that medical education should concentrate on medical work in community settings. This is sound advice yet hard to execute in practice. It is so much easier to monitor standards of medical care in hospitals than in community settings. There is little merit teaching in situations where standards of medical practice are not inspected and approved by faculty. To work well, the staff in community-based medicine and the courses they run must be no less exacting in their standards than those in the hospital-based specialties, and I suspect that it will take time to get it right if only because of the considerable logistic, financial, and other problems. Nevertheless, this is an area where there has been enormous improvement during my academic lifetime. The setting up of university departments of family medicine (general practice), geriatric medicine, mental health, and so on and the appointment to them of staff of first rate ability has transformed the perception of these branches of medicine in the eyes of our students (and perhaps in the eyes of some of our more conservative staff).

Curriculum Style and Organization

Medical Education Should Be Faculty- Rather Than Department-based. The report reflects the widespread feeling that many departments are not really interested in teaching and teach all the wrong things in too great detail (especially preclinical departments); most of us could think of examples to support this. However, it's sad when departments lose responsibility for their teaching since experts in a discipline should know best what contribution their subject can make to the medical course as a whole. Departments should know of the weaknesses and strengths of their own teachers and field these to the best advantage. Departmental teaching should permit better integration since one departmental member should know what the others are meant to be talking about and so reduce overlap or omission. When teaching is organized by departments it should be easier to provide cover for teachers who are ill or on leave. I like to see departments compete with one another to show their subjects in a good light, even if their motivation is only to encourage students to come back to work there later. I like to see them kept on their toes.

Taking responsibility for teaching away from departments is likely to diminish their interest in teaching. Their role in training their own staff in teaching skills is undermined. The groups within faculty who take over responsibility for the organization of the teaching program may not consist of the most prestigious or influential people in the school and this may damage the school's perception of teaching. This, I think, is the crux of the problem. I would like to think that all faculty members should carry some obligation to help plan and deliver student teaching. I don't like to see this important duty left to a small caucus of self-selecting education specialists within faculty.

Medical Education Should Be Integrated Rather Than Subject-based. Though integrated teaching is widely perceived to be a "good thing," and the report comes down on its side, there is often a yawning gap between theory and reality. Almost everyone pays lip service to it yet most people in my experience (except those responsible for it) are not entirely happy with it. I suspect it can be done well if one has enough time, enthusiasm, and resources, but it is not easy. Integrated teaching can be extremely time consuming for the organizers and the teachers (they spend a lot of time in committees) and confusing for the students who have to grapple simultaneously with the different intellectual approaches of a variety of people in different disciplines, and it is bad for departments by removing their responsibility for teaching. Managerially, an integrated curriculum is a complicated curriculum and can result in bureaucratic inflexibility. The philosophy and scientific basis of an individual subject cannot be developed well in an integrated setting, nor is there time to develop historical themes which to me are very important in education.

Staging integrated topic teaching requires enormous managerial skill: marshalling troops, conducting briefing and debriefing sessions, making sure speakers don't contradict one another too much or overrun their times. Even then, the student may only get a series of disconnected mini-lectures lacking a cohesive intellectual theme. The presentations may overlap in content if the presenters do not know which of their points will be given by others. When everyone has spoken and the final panel discussion draws to an end, the show may have outlasted the willingness of the audience to listen. We always hope that next year will be better, but fate may frustrate us if the curriculum committee changes the topic or the organizer goes on leave. It's not for the faint-hearted. Though subject-based teaching can distort proper balance, integrated teaching has much greater capacity for distortion. For most topics, certain disciplines have much greater relevance than others and to give them equal emphasis may not be helpful.

To the outsider, neuroanatomy and neurophysiology seem obvious candidates for integrated presentation, yet the educational case for doing so is not convincing. Neuroanatomists and neurophysiologists can take completely different intellectual approaches to their subjects and to

juxtapose the presentations can confuse the student. Neuroanatomists may see the brain as a structure of beautiful and incredible complexity and describe it as such. The neurophysiologist might prefer to see it as a black box and find the shapes so loved by the anatomist a confusing distraction.

In the end, each student will have to integrate the knowledge he gathers from many sources in a way that makes sense to and satisfies himself. What better integrator could he have for this than his own well-trained brain. If he becomes adept in using it, he will find it a very useful tool to cope with the confusion and anarchy of the real world.

Medical Education Should Be "Active" Rather Than "Passive." The report stresses that medical knowledge is changing so quickly that a student who can't learn independently won't be able to keep up after he leaves university, unless he has learnt to learn by active rather than passive means. My problem with the active/passive concept is that the only learning I know of is the active variety. If there were a technique for "passive" learning which put material into my head at no personal effort, I should use it all the time. It is an effort for me to learn anything and I am grateful for any assistance. For this I will use all the "teaching aids" available, be they books, lectures, diagrams, videocassettes, or, best of all, people who really know what they are talking about. These people are the rarest and best teaching aids and are in heavy demand. It's best if you can have a one-to-one relationship with them but, since there aren't many to go around, it may be necessary for us to form groups to listen to them (say at a lecture) or else read their books or other publications individually. Though these rare people were crucial in helping me to learn in what some might call a passive way, it did not feel passive at the time. My poor brain is easily confused and I had to keep thinking very hard about what I was being told, writing it out and asking questions before I could really come to grips with the material. So I am grateful to people willing to give time for lectures, talks, and writing to assist my learning process. If they were my teachers, I would be sad if they reduced the amount of scheduled time they were prepared to give to help me learn. I need all the help I can get. Left to my own devices without people to explain things to me, I don't think I would have gotten very far, nor perhaps would any isolated member of the human race.

Tosteson[4] made an important point which fits with my experience. He said that people, when asked about the most significant event in their education, usually did not mention a particular course, subject, book, place, or idea. No, in nearly every case they mentioned a person. It is people, not videocassettes, that really influence our mental development. A word—and an honored word—for such people is "Teacher," and they are the most important ingredient in the whole educational exercise. I don't think we should feel ashamed of wanting to influence our students through teaching. To prevent students' being helped by good teachers seems nonsense and contrary to all human history. Independent learning, whatever that may be, can only be a pale and lonely substitute for learning from good teachers who have spent their lives working at and adding to the subject they love. I cannot see that good teaching would limit a student's ability to learn independently in the future and make him mentally lazy. I suspect that it can only increase intellectual curiosity and vitality, which one hopes may be passed on to others. Conversely, in my experience even the most sophisticated and enlightened teaching programs are worse than useless if they are taught or administered by apathetic or disinterested teachers who do not know or love their subject well.

Student Assessment

Evaluation Should Be Subjective as Much as Objective. The urge to switch from objective examinations to subjective evaluation of performance comes from the theory that most examinations test only memorized information and not learning skills. Personally I don't follow this since I suspect that you need to develop learning skills even if only to memorize information. The report states that "standardized examination cannot replace reasoned analytical personal evaluations of the specific skills and overall abilities of the student." I suspect the person who wrote that hadn't much experience of grading large groups of students. Grading a person by what he looks like, says, and does is as fraught with difficulty as attempting to select students by the same method. I have not found it very reliable as judged by the different responses a single student can evoke in different members of staff. I suspect that students, who have a strong feeling for fairness, would want the criteria that determine progress to be reasonably objective. If I were an outsider inspecting a medical school, I would put more weight on an independent objective assessment using objective criteria than on any number of in-house self-evaluations.

Evaluation Should Be Continuous Rather Than Periodic. Some people feel it is unfair to subject students to the emotional stress of important end-of-course examinations in which their progress will be determined based on their ability to reproduce samples of their knowledge. Some consider it kinder to evaluate students by continuous subjective assessment. Unfortunately, with this type of assessment, someone has to watch each student near-continuously to make sure they are doing what the watcher wants. As a system I would hate it. I would prefer to know the objectives required by faculty and have the freedom to meet these in the way that seemed best for me. I wouldn't want my future left in the hands of a faculty member with whose approach to life and work I mightn't agree. I think there is substance in Pickering's[5] criticisms of continuous assessment: (a) if it is properly done, it takes up an enormous amount of staff time, (b) it is virtually impossible to exclude personal bias from the ratings, (c) it does not permit comparison of standards across institutions or countries, and (d) being continually assessed may cause unnecessary anxiety for the students. My greatest worry about it is that making the teacher a constant assessor turns him from being the friend, to help the student learn, into a Big-Brother monitor. The teachers and the taught are put on opposite sides of the system and communication between them is undermined.

I quite like our own arrangement where the teacher's role is to help students reach the national standard required by the licensing body. External examiners are brought in to ensure we maintain these standards in our

end-of-course assessments, and our role is to help the students to satisfy these examiners.

General

Steps Should Be Taken to Define Objectives. Most of us would feel that students should know what they are expected to gain from attending a course and several recommendations in the report urge us to define clearly the objectives of our courses. Few would quarrel with that. Students' anxiety is reduced when they know what faculty expects of them, and it helps them to study. However, unless done with imagination, objectives may become a boring checklist, an imprecise paraphrase of the list of contents in the recommended text. Am I alone in finding lists of objectives so boring to read and to prepare, a tiresome exercise in pedantry? Perhaps I have never come to terms with educational bureaucracy.

Steps Should Be Taken to Increase Resources. There is a theory that most of our difficulties are due to lack of money; that if we had more money for teaching we would teach better and that if we had more research money we would do better research. It is a fashionable cry from those who, like myself, are well practiced in spending public money. However, a lifetime in an education system supported almost entirely by public money has not convinced me that this is always true. In my 30 or so years in the business, our staff-student ratios have improved dramatically, the number of our technicians has gone up exponentially, our department is housed in an imposing medical center instead of in huts, our departmental expenditure is greater in real terms than that which used to support the entire medical school. Yet I am not sure that our teaching is much better, our research is any more exciting, our sense of purpose is any greater, or indeed if we are any happier. With so much plant and personnel to look after, I, as a departmental chairman, spend more time on managerial matters than on the teaching and research I enjoy so much more. I suspect that the university bonanza of the sixties and seventies has given us more apparatus, people, plant, and buildings than most of us can manage properly.

So perhaps I should not join in the chorus for more money from the state. State spending systems tend to encourage waste and may eventually enslave us. I would be happier for the moment making better use of the money I have and, if more is needed, to see how I can earn more from what I do. If no one is willing to pay for what I do, maybe I should be looking for other work. I am not sure that the statement, "undue dependence on faculty generated money inevitably affects educational quality," is always true. It could promote relevance. While saying that, I still feel that some protection of academics from day-to-day and year-to-year financial pressures is essential. Medical research is a tender plant and needs sympathetic patronage. It is prone to wither in a hostile environment.

Steps Should Be Taken to Promote Literacy. There is widespread concern that many young doctors cannot write well and lack the language skills needed to think clearly. I don't know whether or not this is true, but I would still give this recommendation in the report wholehearted approval. It is the key to all education. The only way I know for us to promote it is by giving an enormous amount of time to correct and correct again the literary efforts of ourselves, our students and our colleagues. No one likes having their prose corrected and few of us like to give so much editorial time for such thankless work. However, there is no doubt that the main difference between good writing and bad writing is the amount of time and effort that has been spent on it. Writing is a hard, highly disciplined craft which requires constant practice to maintain quality. It is also a skill where we should all be humble because we have much to be humble about.

Many of us as teachers set bad examples. The *Journal of Medical Education* is not free from verbosity; ideas may be drowned in words and many words are often used where one would do. How can we expect our students to write and think clearly if we write in the style of the following summary taken from a recent paper in an educational journal:

> The authors in this article have described the attempt of one department of family medicine to develop and evaluate a required clerkship which replicates the ethical totality of the patient-family physician relation in effective clinical practice. Special attention has been given to the methodological problem of balancing clinical integration and systematic integrity in such a way as to preserve both the relevance and rigor of ethics in clinical education. A rotation involving both the private practice and academic clinical settings has been combined with an intensive interdisciplinary seminar to develop an appreciation, understanding, and utilization of the biomedical, psychosocial, and valuational components of responsive and responsible ambulatory care.

Another example of indifferent modern scientific prose from a government publication has kindly been brought to my notice by a former colleague, John Shepherd, who now works at the Mayo Clinic. It concerns an empirical classification of U.S. medical schools by institutional dimensions and reads:

> Based on the result of the six factor hierarchical cluster analysis, an optimal solution was sought using Forgy's non-hierarchical cluster analysis method. The results of the hierarchical clustering were used to give an indication of the number of clusters which would represent the schools, and schools were selected as seedpoints for the non-hierarchical cluster analysis based on the hierarchical clusters. In the hierarchical cluster analysis, one school, the Mayo Medical School, appeared so dissimilar from the other 109 schools that it was not included in further comparisons. The Forgy non-hierarchical cluster analysis technique complements the Wörd hierarchical method by optimizing the same criterion, the sum of the squared distances of the schools from the cluster centroids, but does not maintain the permanence of cluster membership inherent in the hierarchical methods.

It is enough to make Flexner turn in his grave; Flexner's report[6] should be required reading for everyone who wishes to write (and think) in medicine. Part of the problem with writing may be that we love our own words so much that having written them down, we cannot bear to throw them out. I suffer from this myself. John Shepherd made me aware of the problem and how he was helped to overcome it. Again, it did not come from attending a course on "how to write good English" but through exposure to the mind of a great teacher. In his early postgraduate days, John produced a magnificent thesis for a certain examination. It was magnificent not only in its findings but in its bulk, with its many fine diagrams and tables. After he was awarded the degree (for which incidentally he also re-

ceived a gold medal), he decided to publish the work. It split conveniently into several sections, each of which he submitted as a separate paper to *Clinical Science*.

George Pickering, who was editor of *Clinical Science* at the time, explained to John how the work could be described with more clarity and force if it were condensed into one short paper and he re-wrote the papers in that form for him. He showed him how to leave out all the words, tables, and pictures that only obscured the central story. One of the pictures to go was a photograph of an ergometer John had designed and built himself and to which he had a strong emotional attachment. Pickering said it was a nice picture which gave some idea of the architecture of the room but little else! This is, of course, very painful stuff at the receiving end but that is what education is about. John Shepherd has had a lasting affection for Pickering, who went to so much trouble and took so much time to help a young author. In my turn, I owe an enormous intellectual debt to John Shepherd, who passed on something of this experience to me. To write briefly is much harder than to write at length, and we cannot blame our students if we set examples of verbosity for them to follow. The hallmark of the scholar should be Flexnerian literacy. Sentences should contain no unnecessary words and paragraphs should have no unnecessary sentences. If there is nothing worth saying, one should stay silent. What better cue to stop.

Conclusions

The GPEP report worries me a bit since it seems to embrace most of the educational fashions of our times whose efficacy in educational terms has not in many cases been proven. Though I'm all for an open mind, I think we should look askance at most new educational theories, no matter how fashionable, in the near-certain knowledge that they are no more (and probably less) likely to be correct than our present ones. No system, no matter how ingenious, is any use if it doesn't work. We would be wise in general to use only those systems where there is a prima facie case that they have worked successfully elsewhere over a period outlasting the enthusiasm of the launchers. There are few prizes and many penalties for being first in medical education. Schools which follow usually do better by benefiting from the trail-blazers' mistakes. Perpetual change for change's sake can undermine morale and efficiency in both students and staff and will make systematic analysis of the effects of change impossible. Evolution seems preferable to revolution as the normal means to progress; there is plenty of time. We do not need to hurry or panic about the year 2000; it is just a number and there are plenty of higher ones. In any event, what the curriculum contains and how it is organized is of much less importance than whether it encourages strong personal bonds of affection and respect, if not love, to develop between the teachers and students and teachers in different disciplines. Only in this context is real education possible. In a medical school it is the people who work there rather than the form of the curriculum that will determine in the end whether it is a good or bad school. I think we would be wiser to channel our efforts to improve medical education into ensuring that the best possible staff will wish to come to teach and research with us rather than have just one more attempt to set the curriculum on its head.

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CORRECTION

In the July issue of the *Journal*, the article entitled, "Medical liability: The perspective of the Medical Liability Mutual Insurance Company" (1986; 86:342–343) contained an error. The first sentence of the next-to-last paragraph should read as follows: Following legislation in July 1985, the New York State Insurance Department proposed that physicians be surcharged according to a merit rating plan that will assign points and surcharges according to a rigid formula based upon paid claims.

Toxic shock syndrome

Case Presentation

Hamid Sadaghdar, MD (Medical Intern): A 35-year-old Chinese woman was admitted for treatment of fever, diarrhea, and abdominal pain of two days' duration. She had previously been well, with no significant illnesses in her medical history. She denied any illness immediately preceding the sudden onset of symptoms. She was not taking any medications. The patient worked as a seamstress. She denied using tobacco or alcohol.

Two days prior to admission, she suddenly developed high fever, epigastric pain, nausea, and diarrhea with eight to ten watery bowel movements per day, together with cough, sore throat, dysuria, and vaginal discharge. She denied having allergies.

On admission the woman appeared mildly agitated, febrile, tachypneic, and acutely ill. Physical examination disclosed the following: blood pressure, 90/60 mm Hg; heart rate, 108/min, respiratory rate, 22/min; and temperature, 104°F. The skin turgor was good; a mild diffuse erythema which blanched on pressure was present, without petechiae or ecchymoses. The conjunctivae were pink and not icteric. A funduscopic examination disclosed no abnormalities. The oral mucous membranes were dry; no oropharyngeal lesions were seen. The lungs were clear on percussion and auscultation. The heart sounds were normal, the rate rapid, and the rhythm regular; there were no murmurs. The abdomen was soft and nontender; the liver and spleen were not palpable. There was a mild increase in audible peristaltic activity. A pelvic examination revealed only a whitish-yellow odorless discharge with blood streaking; the cervix and parametrial areas were not abnormal. The rectum was empty; guaiac test on a small specimen of rectal secretion was negative. The extremities were warm and dry, with mild palmar erythema. The patient was mildly agitated and possibly confused; a language barrier interfered with accurate evaluation. The results of a neurologic examination were entirely negative.

Laboratory tests revealed urine that was yellow and cloudy, with pH 5.0 and specific gravity 1.030; chemical tests showed only a 2+ positive test for protein. Microscopic examination showed five to six white blood cells and four to six red blood cells per high power field.

The hemoglobin level was 12.5 g/dL; hematocrit, 36.1%; white blood cell count, 21,500/μL, with 54% polymorphonuclear leukocytes, 40% band forms, 2% lymphocytes, and 4% monocytes. The platelet count was 382,000/μL; prothrombin time, 14.6 sec (control 12.2 sec); and partial thromboplastin time, 32.8 sec (control 26.4 sec). The blood urea nitrogen level was 34 mg/dL; creatinine, 2.6 mg/dL; blood glucose, 136 g/dL; and serum amylase, 12 units/mL (normal, 4–25 U/mL). The serum electrolyte levels were as follows: sodium, 132 millosmoles/L; potassium, 3.0 mmol/L; chloride, 97 mmol/L; and bicarbonate content, 18 mmol/L. Arterial blood gas determinations with the patient breathing room air yielded pH, 7.38; P_{CO_2}, 28 mm Hg; P_{O_2}, 121 mm Hg; bicarbonate content, 14 mmol/L; base excess minus 14 mmol/L; and oxygen saturation, 98%. A pregnancy test was negative.

Initial bacteriologic cultures were obtained from the pharynx, blood, urine, stool, rectum, and vagina. A Gram's stain of the vaginal secretions showed a few polymorphonuclear leukocytes and many gram-positive cocci.

A chest radiograph showed a normal cardiac silhouette, with no pulmonary infiltration or effusions (Fig 1). Plain radiographs of the abdomen showed only multiple air-fluid levels with the patient in lateral decubitus positions.

An electrocardiogram showed a sinus tachycardia with a PR interval of 160 milliseconds, a QRS interval of 84 milliseconds, an axis deviation of plus 77 degrees, and negative T waves in leads II, III, aVF, and precordial leads V-1 through V-6 (Fig 2).

The initial clinical impression was sepsis, probably secondary to gastroenteritis. Monitoring of urine flow with a Foley catheter showed a very low initial output.

On the night of admission, the patient was given ampicillin, an initial loading dose of gentamicin, and clindamy-

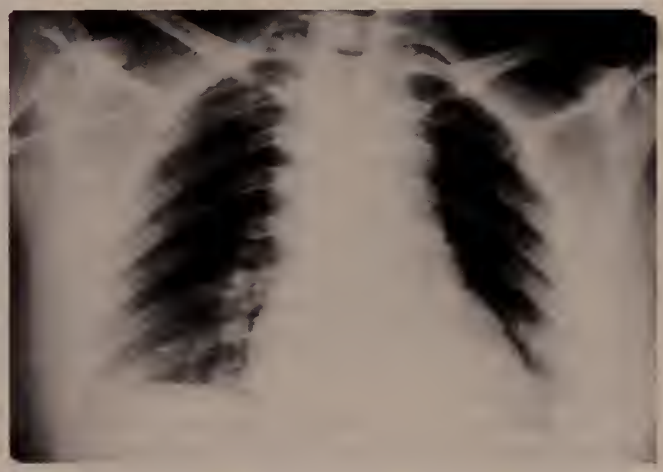

FIGURE 1. Chest radiograph taken on admission shows normal heart and lungs.

Based on a clinical conference held at the New York Infirmary, Beekman Downtown Hospital, New York City, on March 7, 1986.
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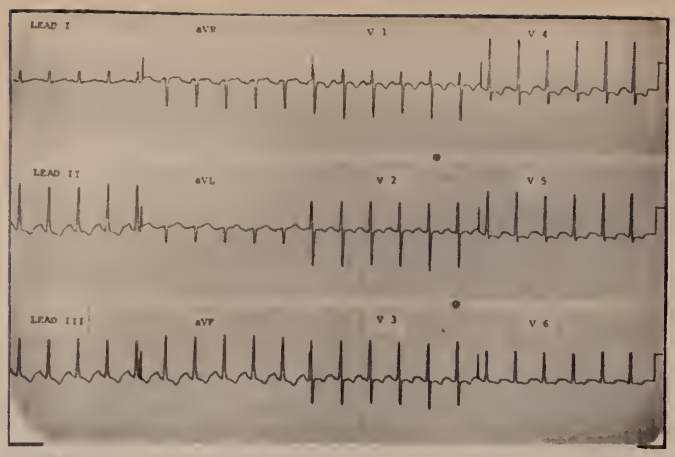

FIGURE 2. Electrocardiogram taken on admission shows sinus tachycardia and negative T-waves in leads II, III, aVF, and all precordial leads.

cin; despite 200–600 cc of fluid administered per hour, the patient's blood pressure fell to 60/40 mm Hg. In view of high fever, tachypnea, and continued oliguria, the patient was transferred to the Medical Intensive Care Unit.

The next morning, the patient's diffuse skin rash had intensified and now appeared to be an erythroderma. Repeat pelvic examination by the gynecologic consultant was negative, except for the finding of fresh blood compatible with active menstruation, which was confirmed on further questioning through an interpreter.

At this time, the blood calcium level was 7 mg/dL; phosphate, 2 mg/dL; serum aspartate aminotransferase (AST; SGOT), 103 U/L (normal range, 10–40 U/L); alanine aminotransferase (ALT; SGOT), 45 U/L (normal range, 1–21 U/L). The prothrombin time had increased to 18.2 sec (control, 12.2 sec) and the partial thromboplastin time to 51.2 sec (control, 27 sec). A test for serum fibrin split-products was positive in dilution above 1:40 (normal, negative reaction at greater than 1:4 dilution). The patient's hemoglobin level was now 8.8 g/dL, and the hematocrit was 27%. The serum creatine phosphokinase level was 7,840 U/L (normal range in women, 5–35 U/L).

The acute onset of fever, low blood pressure, oliguria, diffuse erythroderma, leukocytosis with a left shift, and disturbance of the clotting mechanism in a young menstruating female patient suggested a diagnosis of toxic shock syndrome. Oxacillin, 2 g, was given every six hours, together with other supportive measures. By the afternoon of the first hospital day, the patient showed rapid improvement.

During the next three days, the patient's temperature and heart rate gradually returned to normal; simultaneously, however, her skin underwent extensive desquamation—mildly over the face, but markedly over the hands.

All initial bacteriologic cultures were negative, except for the growth of *Staphylococcus aureus* and *Escherichia coli* in cultures of the vaginal secretions. Following antibiotic therapy, repeat vaginal cultures showed only *E coli*.

The final diagnosis was toxic shock syndrome of undetermined cause.

Naveen Rao, MD (Attending Physician): You have not mentioned the possibility of vaginal tampon use.

Dr Sadaghdar: Initially we had no background information at all. And our only later source of information was a relative who said that the patient did not use tampons but only pads during her menses.

John T. Flynn, MD (Associate Chief of Medicine): On the pelvic examination, was there any evidence of retained tampon material or any other foreign material in the vagina?

Dr Sadaghdar: The gynecologist's examination during the first hospital day was entirely negative; no foreign material of any kind was seen.

James Rahal, MD (Chief, Division of Infectious Diseases): My examination of the patient indicated the conjunctivae were quite red, and that she had mucous membrane involvement.

Dr Sadaghdar: We did not see that at the time of the patient's admission.

Robert Appel, MD (Attending Physician): What significance did you give to the air-fluid levels on the x-ray of the abdomen?

Dr Sadaghdar: We thought they represented a pattern of mild ileus. The surgical consultant agreed with us at the time that they did not indicate the presence of serious intestinal obstruction and that surgery was not indicated.

George Braff, MD: (Director of Radiology): On the chest film taken on admission, the lungs appear clear; the heart size is within the normal range (Fig 1). On the third hospital day, the chest film shows some dilation of the pulmonary vasculature and haziness, especially at the right lung base (Fig 3). There is a suggestion of Kerley B lines, and possibly some pleural fluid bilaterally. Fluid overload or congestive failure due to shock had to be considered.

Two series of abdominal films show scattered small-bowel gas in a nonspecific pattern. A J-shaped gas pattern in the same loop of bowel would suggest an obstructive process, while the inverted U-shaped pattern which we see on these films would suggest an adynamic ileus pattern which can be seen in gastroenteritis.

Irwin Sharkey, MD (Chief of Medicine): Dr Sadaghdar, how did that second chest x-ray influence your thinking?

Dr Sadaghdar: We were very concerned that the patient might be developing acute respiratory distress syndrome (ARDS), so we decreased the intravenous fluids. However, even at the time of this second film, the patient's lungs were entirely clear on physical examination.

FIGURE 3. Chest film taken on third hospital day, showing dilated pulmonary vasculature, pulmonary congestion, and possible bilateral pleural effusions.

Dr Sharkey: What did the arterial blood gas determinations show?

Dr Sadaghdar: The daily determinations were all normal except for a single Po_2 of 52 mm Hg; the pH determinations initially suggested a mild acidosis.

Harry Taube, MD (Attending Cardiologist): Did the electrocardiogram show any further changes?

Dr. Sadaghdar: Initially, we interpreted the T-wave abnormalities in leads II, III, and aVF and in precordial leads V-1 to V-6 as secondary to the marked tachycardia of 140/min. But as late as ten days after admission, some of the T-wave changes persisted, in spite of a slower pulse rate (Fig 4).

Paul Bellman, MD (Medical Resident): With this suggestion of congestive failure and the EKG changes, how did you interpret the changes in the serum creatine phosphokinase (CPK) levels?

Dr Sadaghdar: That was difficult. Damage to skeletal muscle in toxic shock syndrome can cause a marked elevation of CPK, to many thousands of units per liter. We thought that this explained the marked increase in the CPK, since the patient had no cardiac symptoms—no shortness of breath or chest pain; the lungs remained clear, and the physical findings were negative.

Review of Differential Diagnosis

Richard Slubowski, MD (Medical Resident): At the time of this patient's admission, the diagnosis of toxic shock syndrome was not at all obvious. In addition, a language barrier limited the information available to us.

This patient had a completely negative past medical history and was not taking medications. The sudden onset of symptoms two days prior to admission—fever, epigastric pain, vomiting, diarrhea, sore throat, cough, dysuria, and vaginal discharge—could all easily be due to a viral syndrome. The physical examination indicated high fever, tachycardia, hypotension, no initial evidence of a skin rash, and no physical findings suggestive of a localized infection. The pelvic examination showed vaginal secretion but no tenderness or pelvic masses. There was little evidence of active menstruation, and she had not been using tampons.

Laboratory studies showed an elevated white blood cell count with a marked left shift, increased blood urea nitrogen and creatinine levels, and serum bicarbonate content compatible with mild acidosis. The blood smear showed fragmentation of the red blood cells, which, together with the abnormal coagulation profile, suggested disseminated intravascular coagulation (DIC).

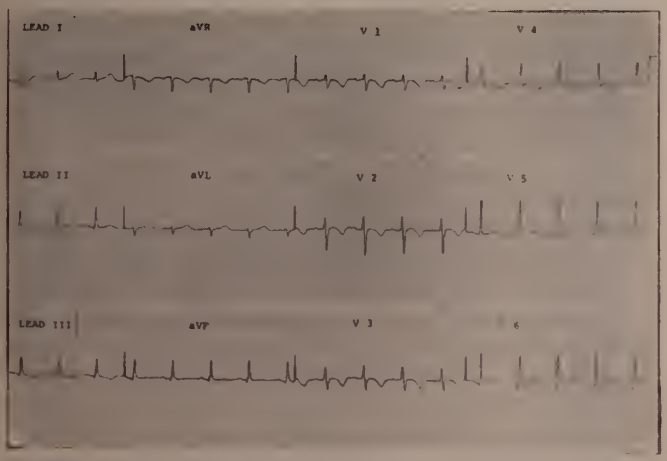

FIGURE 4. Electrocardiogram taken ten days after admission, showing negative T-waves in leads V-1 to V-4.

We initially suspected a bacterial infection, most likely gastroenteritis due to *Shigella* or *Salmonella*, or to an enteropathic *E coli*.

Shigella gastroenteritis has a short incubation period, followed by fever, abdominal pain, diarrhea, nausea, vomiting, myalgia, and headache. The stools are often greenish and bloody. Stool cultures, when obtained early, are positive in 90% of cases; blood cultures are rarely positive. At times, *Shigella* infections can be complicated by the hemolytic uremic syndrome; but ordinarily the infection is self-limited and lasts four or five days. During outbreaks, the illness is more fulminant.

Salmonella infection typically has a prodrome, with headache, malaise, fever, and sometimes cough. Thereafter, abdominal symptoms and diarrhea appear; disseminated intravascular coagulation may occur in such cases. Bradycardia and leukopenia, in the absence of intestinal perforation or other complications, are characteristic. In typhoid, the blood culture is positive in 79% of cases early in the clinical course; stool cultures are positive in 10–15% of cases. In salmonellosis, rose spots, which are small erythematous macules, may be seen on the upper extremities and on the abdomen.

The morning after admission, this patient's skin rash became more evident, and the presumptive diagnosis of gastroenteritis had to be reassessed. Toxic shock was then considered, along with rickettsial diseases such as typhus and Rocky Mountain spotted fever.

Typhus will cause malaise, headache, fever, myalgia, nausea, vomiting, and diarrhea; a maculopapular rash usually appears on the fourth to the seventh day, characteristically over the trunk and axillary folds, but sparing the palms and soles. Rocky Mountain spotted fever presents with similar symptoms, but the rash also involves the palms and soles. These dermatologic characteristics did not correspond to what we were seeing in this patient. And neither typhus nor Rocky Mountain spotted fever causes such a marked elevation of the white blood cell count.

In gonococcemia, the rash usually consists of a few pustules located peripherally on the extremities; tenosynovitis and arthritis are prominent clinical findings. Blood cultures are usually positive early in the infection.

In meningococcemia the rash is usually petechial in character, and may progress to ecchymoses and necrosis of the skin of the extremities.

Kawasaki disease usually occurs in children, and presents with fever, redness of the lips and conjunctivae, erythema of the palms and soles, desquamation of the fingers, and rashes over the trunk. Interestingly, this initial diagnosis reported in some adult patients was subsequently changed to that of toxic shock syndrome.

Kawasaki disease is characterized by prominent cervical lymphadenopathy and has a more prolonged course than toxic shock syndrome, sometimes with serious cardiovascular complications.

Leptospirosis can cause fever, headache, myalgia, nausea, vomiting, abdominal pain, cough, increased white blood cell count, decrease in platelets, abnormal liver en-

zyme levels, and increasing renal failure. Typically, the patient is hypotensive, with a relative bradycardia. However, leptospirosis usually occurs in sewer workers or others who come into contact with fecal material from rats, sometimes by swimming in infected water. The organism must be grown on Fletcher's medium, preferrably in blood culture. This patient presented no risk factors for this disease.

The onset of toxic shock syndrome can mimic that of gastroenteritis, pelvic inflammatory disease, pyelonephritis, and scarlet fever, as well as other streptococcal and staphylococcal infections. Toxic shock syndrome seemed the most probable diagnosis in this patient, when *Staphylococcus aureus* was found in cultures of the vaginal secretions; cultures of urine, stool, and blood were all negative. Toxic shock syndrome is not associated with bacteremia or septicemia, but apparently with systemic absorption of a locally produced toxin that leads to the symptoms.

Dr Sharkey: What was the rationale for the initial early use of antibiotics?

Dr Slubowski: We were concerned about the possibility of a gram-negative septicemia.

Dr Rao: How long was the oxacillin continued?

Dr Slubowski: It was administered for eight to ten days. That may be considered excessive if only a local staphylococcal growth in the vagina were the cause of this syndrome. But in atypical cases, in which a localized staphylococcal infection such as an abscess might be responsible, a longer course of antibiotic therapy would be indicated, in addition to possible surgical drainage. Admittedly, that kind of infection would be more common in male patients.

Dr Rao: Is the vaginal tampon colonized by the staphylococcus?

Dr Slubowski: That may happen, but there can be overgrowth of *Staphylococcus aureus* in the vagina without the presence of a tampon at any time.

Satish Dhalla, MD (Attending Physician): When I saw the rash on the fifth or sixth day, the excessive desquamation was typical of toxic shock syndrome. The various cultures were not yet fully observed and reported, so that the use of antibiotics was to some extent still uncertain.

Other confusing and atypical features were the lack of use of a tampon, and the absence of a history of menstruation prior to the onset of symptoms. Also the fragmentation of red blood cells, prolonged prothrombin and partial thromboplastin times, and the increased serum fibrin split-products were all evidence of disseminated intravascular coagulation, which is a rare complication of toxic shock syndrome. Nausea, vomiting, and diarrhea can occur but are also not the most common presenting features.

Dr Slubowski: The sloughing of skin had extended over the palms and soles; in some patients this can go on to gangrene of an entire finger.

Dr Rahal: It is extremely rare to experience such sloughing of the skin except in scarlet fever and in toxic shock syndrome.

Review of Toxic Shock Syndrome

Alice M. Freudenthal, MD (Chief Medical Resident): Before 1977, what corresponds to toxic shock syndrome was called staphylococcal scarlet fever.[1] In 1978, Todd described toxic shock syndrome in children 8 to 17 years of age; in all these cases, he isolated a staphylococcus, bacteriophage group I and III, from skin abscesses, empyema fluids, mucous membranes, or vaginal secretions.[2]

By 1980, this syndrome became prominently related to the use of tampons during menses. After 38 such cases were reported from Wisconsin,[3] the Centers for Disease Control (CDC) monitored cases and made retrospective and prospective evaluations. Shortly thereafter, tampons said to be associated with the syndrome were withdrawn from public sale.

By April 1984, a total of 2,509 cases of toxic shock syndrome had been reported from all 50 states[4]—95% in women and 5% in men, with 97% in Caucasians. Eighty-nine percent of the patients were menstruating at the time of illness; 99% of these cases were associated with the use of tampons. Other cases in which the patient was menstruating were also associated with the use of sponges and napkins.

Cases of toxic shock syndrome not associated with menstruation have been reported in the postoperative period; with Caesarean sections; with *Staphylococcus aureus* vaginal infections during the postpartum period; and with wound infections, mastitis, and surgical incisions in nearly every location, including osteoplasties and nasal surgery with packing. Superficial *Staphylococcus aureus* infections also have been involved, including infected burns, furuncles, abscesses, abrasions, and insect bites. Septic arthritis, sinusitis, bursitis, osteomyelitis, empyema, and prostatitis have been implicated. But the most treacherous form of toxic shock sydrome occurs in the presence of colonization by *Staphylococcus*, without evidence of infection.

Persons of all ages and both sexes have been victims of the syndrome.

The incidence of cases not associated with menstruation increased progressively from 7% in 1980 to 29% in 1983, reflecting perhaps the decrease in the reported cases associated with menses and tampon use.

Since 1981, protein substances suspected of being toxins have been isolated from a high percentage of *Staphylococcus aureus* strains in patients with toxic shock syndrome.[5] Such substances have stimulated some of the symptoms of toxic shock syndrome in animals and have demonstrated other significant biological activity, including stimulation of interleukin-1, alteration of lymphocyte function, and suppression of immunoglobulin (Ig) M antibody synthesis. No one of these substances has been able to produce the full-blown syndrome when injected into animals; and the presence of other as-yet-unidentified "toxins" is reasonable to expect.[6]

In vitro, the production of one such toxin (toxic shock syndrome toxin-1, or TSST-1) is controlled by the magnesium content of the medium.[7] It has been suggested that the fibers of the vaginal tampons associated with this disease chelate magnesium from vaginal secretions, decreasing its concentration in vaginal secretions and thus secondarily permitting the increased production of the toxin.[8]

The definition of toxic shock syndrome includes six criteria, almost all of which are evident in this patient: fever; a diffuse macular erythroderma; subsequent desquamation, especially of palms and soles; hypotension, with or

without orthostasis and dizziness; multisystem involvement—skeletal muscle, gastrointestinal tract, mucous membranes, central nervous system, kidneys, liver, and bone marrow, with thrombocytopenia and disseminated intravascular coagulation. Finally, cultures of bodily fluids do not indicate other bacterial infections, and there is no serologic evidence of other viral, rickettsial, or spirochetal diseases.

Electrocardiographic changes can occur—new onset of second or third degree heart block, changes in the ST segments and T waves, or heart failure, for example—all secondary to a carditis.

One needs to have a high level of suspicion in order to diagnose toxic shock syndrome, especially in patients in whom a surgical wound shows no physical signs of infection, but appropriate cultures will identify the presence of the staphylococcal organisms.

Menstruating patients with toxic shock syndrome are usually young. They present with acute illness, including a prodrome of malaise, weakness, and fever. They usually enter the hospital within 48 hours and require seven or eight days of hospital care. There is a rapid shift of fluid from the intravascular to the extravascular compartment, with resulting hypotension and oliguria. The rash, central nervous system changes, and other symptoms follow. The patient requires admission to a Medical Intensive Care Unit, with close monitoring of vital signs and repeated evaluations of urine output, blood counts, and capillary wedge pressure. Periodic chest radiographs, arterial blood gas determinations, and blood chemistries, including serum calcium, phosphorus, and magnesium, are needed.

The complete blood count will often show anemia, leukocytosis with absolute lymphopenia, and thrombocytopenia; the coagulation profile often shows prolonged prothrombin and partial thromboplastin times, and increased serum fibrin split-products, suggesting disseminated intravascular coagulation.[9] The BUN and serum creatinine levels are often increased, and liver function tests are abnormal. The decreases in total calcium and ionized calcium levels may be related to the low level of serum magnesium and to the high amount of immunoreactive calcitonin.

In 100% of patients, at least one of the cultured specimens will grow *Staphylococcus aureus*, though not from the blood. Sometimes, of course, there may be a bacteremia for other reasons. Up to 17% of women carry *Staphylococcus aureus* in the vagina, and this may produce the toxin in special circumstances.

After admission to the Intensive Care Unit, the patient usually requires intravenous fluids and, sometimes, vasopressors, as well as a beta lactam-resistant penicillin to eradicate the toxin-producing *Staphylococcus*. Patients who are not treated with antibiotics tend to have recurrences of the syndrome during subsequent menstrual periods, and these must be prevented.[3,10]

Vaginal tampons must be removed, abscesses incised and drained, and appropriate antibiotics used. Steroid and calcium therapy may be used, but the latter may not be necessary. When the hypotension is refractory, parenteral calcium can sometimes help; but further studies are required to elucidate the therapeutic role of calcium in these patients.[11,12]

The patient must be observed for the development of acute respiratory distress syndrome, hypertension, or acute renal failure. These complications are the same whether or not the patient is menstruating. Late sequelae include a delayed antibiotic-related rash, chronic renal failure, neuromuscular disorders, and cyanotic extremities.

Dr Rahal: The question was raised as to why this syndrome occurred in the absence of tampon use. Toxin production by *Staphylococcus* can occur with colonization alone and does not require infection. The tampon alone does not cause the syndrome; the entire clinical picture can occur due to staphylococci proliferating in a surgical wound or elsewhere. Most of the surgical cases, interestingly enough, have been associated with packing, which may serve the same role as the tampon.

Approximately 10% of women ordinarily carry *Staphylococcus aureus* in the vagina, some organisms being toxigenic and some not; many women carrying toxigenic *Staphylococcus aureus* remain asymptomatic. If there is only colonization of staphylococci in the vagina, why does the organism sometimes suddenly begin to produce toxin? In the absence of actual infection, the tampon no doubt plays a role, mostly as an inciting factor.

Dr Bergdoll at the University of Wisconsin secured data on this matter. Drs Tierno and Hanna at New York University repeated Dr Bergdoll's experiments[8] and showed that highly absorbent tampons that contain carboxymethylcellulose or similar polymers can significantly increase the production of toxin by the staphylococci. Certain tampons may also affect the amount of local magnesium available, which appears to regulate toxin production. It is likely that certain tampon components are responsible for enhancement of toxin production, since this syndrome occurs statistically less often in patients who use the old-fashioned, less absorbent cotton tampon.

In the absence of a tampon, it is hard to explain why the staphylococci colonizing the vagina would produce enough toxin to cause the syndrome, unless the patient had a vaginitis with actual bacterial invasion of the vagina.

This case illustrates very well the value of a Gram's stain in evaluating what first appeared to be a normal whitish vaginal secretion. If the Gram's stain of this discharge showed polymorphonuclear leukocytes and staphylococci, you could say that this patient did not require a tampon in order to develop the staphylococcal toxic shock syndrome.

Ordinarily one would not expect to find polymorphonuclear leukocytes in normal vaginal secretions, as Dr Sadaghdar did in this case. If there were sufficient numbers of staphylococci so that they were seen on the Gram's stain, then there were sufficient staphylococci to produce this disease.

In connection with the patient's diarrhea, Gram's stain of the stool can be helpful in evaluating the underlying cause. One easy way to identify a bacillary invasive dysentery, due for example to *Shigella* or *Salmonella*, is to find white blood cells in the stool on Gram's stain. These would not be present in the stool in a toxigenic dysentery, of which the prototype is cholera, and which is most probably the type occurring in the staphylococcal toxic shock syndrome.

Dr Sadaghdar: The rectum was entirely empty and there was no stool to smear and to test with a Gram's stain.

Dr Rahal: If you saw white blood cells in the stool and none in the vaginal secretion, you would have one diagnosis—probable bacillary enteritis; staphylococci and white blood cells in the vagina but not in the stool would point to a different diagnosis—toxic shock syndrome.

It is important to comment on the methicillin-resistant *Staphylococcus aureus*. Once resistant to methicillin, *Staphylococcus* will be resistant to many other antibiotics. At one time, staphylococcal enteritis could be treated effectively by almost any antibiotic. But with methicillin-resistant staphylococci, we may be faced with a return of this form of enteritis—another reason to use Gram's stain to test the stools of all patients with a diarrheal syndrome. In addition to white blood cells in bacillary enteritides, one may find a predominance of gram-positive cocci in clusters, or perhaps yeast, indicating either staphylococcal or candidal enteritis. In clinical circumstances like these, do not think only of pseudomembranous enterocolitis, just because it is currently fashionable to do so.

In the 1930s, it was known that both the group A streptococcus and *Staphylococcus aureus* could produce scarlet fever.[1] The only major difference between the two types of illnesses was the lack of a pharyngitis in cases caused by staphylococci. Positive cultures for staphylococci can be obtained from almost anyone's throat; but those organisms will not cause a pharyngitis. However, both staphylococci and streptococci can produce similar erythrogenic toxins. Thus, the only major difference between the two types of scarlet fever is that the streptococci proliferate and invade the throat, while the staphylococci localize elsewhere, most often in a surgical wound. In toxic shock syndrome, elevation of the serum creatine phosphokinase level because of muscle involvement is a very helpful indicator of the syndrome.

Toxic shock syndrome has some resemblance to scarlet fever, a disease which has nearly disappeared. The type of rash in the two conditions is similar—a vascular erythroderma which is confluent and blanches on pressure. The engorged skin papillae result in a palpable rash. When the patient loses fluid because of diarrhea, has high fever and an accompanying flush, and is hypotensive, it is very easy to overlook the rash. Even if a rash is not noted clinically but desquamation occurs later, it means that a rash has been present.

Increased capillary fragility with this type of rash was evident in one patient by the appearance of ecchymoses in the areas where electrocardiograph leads were placed by suction over the anterior chest wall. Also, in scarlet fever and in toxic shock syndrome, there may be Pastia's lines, which represent the disruption of the fragile capillaries in the anticubital fossa when the arm is bent. Capillary fragility is so great in scarlet fever that purpura can be found over the lower extremities. Desquamation occurs late in scarlet fever, as well as in toxic shock syndrome.

This type of rash and desquamation can occur as a side-effect of sulfonamides and other drugs, but this is not a frequent occurrence. Following any surgical procedure, a patient may develop high fever and be treated with a beta-lactam antibiotic such as ampicillin. Thereafter, a rash may appear which is often blamed on the medication. However, beta-lactam antibiotics usually do not produce a confluent erythematous blanching rash similar to that seen in toxic shock syndrome or scarlet fever. The surgical wound should be cultured, and, if *Staphylcoccus aureus* is found, it is possible that the patient may have developed a *Staphylococcus aureus* wound infection and staphylococcal scarlet fever. Staphylococcal scarlet fever is caused by an erythrogenic toxin and does not present with diarrhea and hypotension as does toxic shock syndrome associated with toxic shock syndrome toxin-1 (TSST-1).

We know little about the processes that encourage staphylococci to produce this erythrogenic toxin or the TSST-1 or possibly both toxins. It is not clear whether TSST-1 can produce the rash. Thus, we do not know whether one toxin alone or two together produce the entire syndrome. There is also some evidence that endotoxin from gram-negative bacilli may act in concert with TSST-1 to produce the syndrome.

Criteria for toxic shock syndrome do not include the necessity for isolating *Staphylococcus aureus* on culture. We are continuing to learn what organisms may cause this disorder. The criteria established by the Centers for Disease Control are meant only to define the condition as a syndrome, possibly caused by a variety of organisms and their toxins.[13]

Whenever one sees a syndrome that lacks a specific diagnostic test, one can argue forever about whether a patient has it or not. One can pick apart each criterion; and any number of criteria can be required to make the diagnosis. With any syndrome, one will find cases at both extremes of the spectrum. The criteria for a syndrome are assembled largely for epidemiologic purposes. But nature does not put together a syndrome along the lines of a fixed and exact set of symptoms and signs. There are probably many mild cases of toxic shock syndrome, which are evanescent and consequently are rarely diagnosed.

Many women who have had toxic shock syndrome experience subsequent minor episodes of diarrhea and muscle aching, or give a history of the condition in connection with several menstrual periods in the past.[10] These less obvious instances of this syndrome must await the development of a specific test with which we can make an accurate diagnosis.

Dr Dhalla: Has toxic shock syndrome appeared in the setting of staphylococcal food poisoning?

Dr Rahal: Staphylococcal food poisoning is due to different enterotoxins. Bergdoll[14] found enterotoxin F by culturing the organism, removing the supernatant, and separating the protein fractions. He then compared the protein groupings against standards that identified the toxins that cause the food poisoning—A through E. This method indicated that the cultured staphylococci had produced a toxin which migrated differently from the A through E toxins, so he labelled it F and believed it to be the cause of toxic shock syndrome.

The staphylococci that produce toxic shock syndrome may not produce the other enterotoxins. Similarly, the organisms that cause food poisoning, very likely by means of the A-through-E toxins, may not produce toxic shock syndrome toxin F.

Bart Kummer, MD (Attending Physician): Is there any seasonal incidence or variation to the nonmenstrual forms

of this disease, during or after the flu season, for example?

Dr Rahal: I do not know about a seasonal incidence. We see more staphylococcal respiratory infections during the influenza season, but all year long we are seeing all kinds of staphylococcal infections. The additional cases during an influenza outbreak may not be sufficient to create a seasonal incidence.

It is of great interest that the CDC has reported cases of toxic shock syndrome occurring for the first time in association with influenza, in Minnesota during February 1986.[15] Such patients had influenza, TSST-1-producing *Staphylococcus aureus* in the sputum, and hypotension with bacteremia, together with fever and late desquamation. This is consistent with the ability of such strains of *Staphylococcus aureus* to cause toxic shock syndrome with infection, or merely with colonization of any one of several bodily locations.

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PICTURE OF THE MONTH

Family Stroll. Canadian geese (Kenneth A. Deitcher, MD). Taken with a Canon A1 with a Vivitar 70–210 macro-zoom lens, f16, 1/125 second.

The *Journal* is inaugurating a new feature of publishing suitable photographs. Entries should be submitted as 5″ × 7″ black and white glossy prints, along with a brief caption and information concerning the camera and lens used, *f* stop, and shutter speed.

Thrombocytopenic purpura and infectious mononucleosis

A possible role for high dose intravenous immunoglobulin

ALAN E. RAUCH, MD, WILLIAM B. SCHARFMAN, MD

Although mild thrombocytopenia in patients with infectious mononucleosis is not uncommon,[1] the incidence of severe thrombocytopenia has been reported as less than 1% of all cases.[2] Severe thrombocytopenia may be life threatening and may be the most significant complication of this disease. There are various methods of therapy, including the administration of steroids and splenectomy. We report a case of severe thrombocytopenia associated with infectious mononucleosis which responded to high dose intravenous immunoglobulin.

CASE REPORT

A 17-year-old woman was admitted to the Albany Medical Center Hospital with bleeding gums, epistaxis, and a petechial rash of one day's duration. She had had persistent menorrhagia and a single episode of epistaxis one week prior to admission, and a mild flu-like illness several weeks previously, with excessive fatigue. She denied sore throat or painful adenopathy. There was no history of drug or alcohol abuse.

A physical examination revealed petechial hemorrhage of the oral mucosa and the lower extremities. There was a 1 × 1 cm lymph node in the left anterior cervical chain which was slightly tender. The spleen was not palpable.

Laboratory data on admission showed a hemoglobin of 13.5 g/dL; hematocrit, 40.5%; leukocyte count, 19,300/μL with 23 neutrophils, 10 band forms, 40 lymphocytes, 3 monocytes, 1 eosinophil, and 23 atypical lymphocytes. The platelet count was 1,000/μL. The peripheral smear showed an increased number of atypical lymphocytes and no platelets. The prothrombin and partial thromboplastin times were within normal limits, and the Coombs' direct and indirect tests were negative. Tests for antinuclear antibody (ANA), rheumatoid factor, and VDRL were negative, and the liver function tests were normal. A Monospot test was positive.

Because of continued epistaxis and persistent petechial hemorrhage, the patient received a transfusion with eight units of random donor platelets, without a rise in platelet count. In addition, she was given 80 mg of methylprednisolone intravenously, and then started on prednisone, 15 mg four times a day. A bone marrow aspirate revealed increased numbers of megakaryocytes and a small population of large cells that resembled atypical lymphocytes. The patient's platelet count during her hospital stay is shown in Figure 1. By the seventh hospital day, there was no change in the platelet count; the menorrhagia and epistaxis continued. High dose intravenous immunoglobulin 400 mg/kg/day was then started and was continued for five days. By the fifth day, there was a significant rise in the platelet count. The patient was able to be discharged one week later with a platelet count of 80,000/μL. Her platelet count quickly returned to normal ten days after completing the immunoglobulin on an outpatient basis; the prednisone was tapered rapidly. Follow-up for ten months has indicated a continued remission.

DISCUSSION

This patient had thrombocytopenia as supported by the increased number of megakaryocytes in the bone marrow and the lack of response to the initial platelet transfusion. The absence of any drug use, negative findings on an ANA test, lack of recent transfusion, presence of atypical lymphocytes, and positive Monospot test support the diagnosis of infectious mononucleosis and suggest that it is probably the cause of the thrombocytopenic purpura. Although this was the sole clinical manifestation of the infectious mononucleosis, similar findings have been reported previously.[3] Steroid therapy was start-

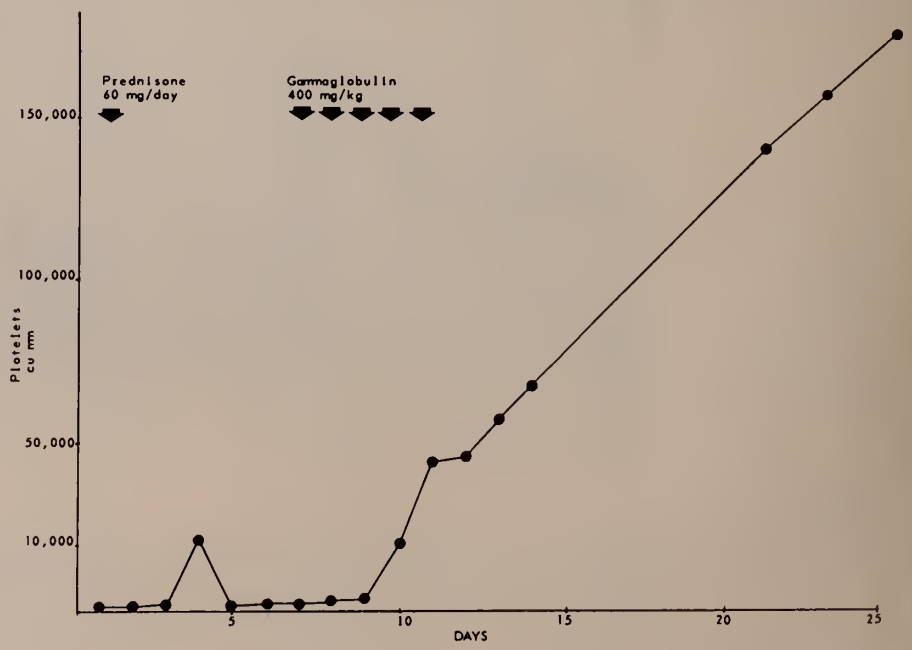

FIGURE 1. Serial changes in platelet count.

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ed immediately but failed to improve the clinical course after one week. Administration of high dose intravenous immunoglobulin was then considered. The patient responded to this treatment; her platelet count steadily improved. Normal platelet levels were maintained as the prednisone was discontinued.

Thrombocytopenic purpura associated with infectious mononucleosis was originally described in 1942.[4] A review of the literature in 1975 revealed fewer than 40 reported cases[5] with an incidence of less than 1%, suggesting the rarity[6] of this complication.

The pathogenesis of the thrombocytopenia is not clear, although it is suspected to be an antibody-mediated process. The platelet-associated antigen is probably either secondary to the Epstein-Barr virus or an autoantigen. Whether other immune mechanisms are mediated through haptens or through an innocent bystander, or are idiosyncratic, is not known. Abnormalities of the immune system that allow for development of an antiplatelet antibody have also not been determined, although disturbance of immune regulation may occur in viral infections. Epstein-Barr virus is a polyclonal B cell activator and could be responsible for production of autoantibody in this patient. In addition, most of the atypical lymphocytes in infectious mononucleosis are T cells[7] and, arguably, suppressor cells.[8] If an autoantibody is involved in the thrombocytopenia, this may be secondary to a defect in immune regulation, possibly involving suppressor T cells.[8]

The mechanism by which high dose intravenous immunoglobulin improves thrombocytopenia is also not known. The most likely mechanism is a blockade of the macrophage Fc receptor, resulting in decreased immune clearance.[9] Other possibilities include inactivation or inhibition of circulating antiplatelet antibody synthesis or interference with attachment of intrinsically produced immunoglobulin, which is responsible for platelet removal.[10] Also, the activation of T cells and suppression of B cells has been postulated to inactivate a circulating antiplatelet factor.[11]

Whether the improvement in this case was secondary to steroid therapy, high dose intravenous immunoglobulin, or was coincidental is not known. However, other studies have suggested a longer course before spontaneous improvement[3,5]—as long as six months. Steroid therapy used alone to treat thrombocytopenia associated with infectious mononucleosis has not produced an appreciable platelet response,[5] with elevated counts not occurring until four to six weeks after treatment is initiated. This seems to indicate that the immunoglobulin and/or steroid therapy was helpful. Indeed, when compared,[12] immunoglobulin therapy appears to be more efficacious than steroid treatment, suggesting a causal relationship between the immunoglobulin therapy and the improved platelet count. Use of high dose intravenous immunoglobulin therapy should be considered for the patient with severe thrombocytopenia associated with infectious mononucleosis.

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Torsion of an ovarian cyst in a premature infant

Barnett M. Miller, MD, Adolfo A. Trocino, MD, Anup Gheewala, MD

Ovarian cysts and neoplasms are recognized entities in the pediatric age group, but are relatively rare in the neonate. Even more uncommon in the neonate is a clinical picture in which the ovarian mass becomes associated with such problems as rupture, hemorrhage, intestinal obstruction, or volvulus.

In the case presented, an abdominal mass of undetermined etiology was noted at birth in a premature female infant. Attempts to establish a definitive diagnosis were unsuccessful, despite the utilization of barium enema, radionuclide scintigraphy, ultrasonography, and computed tomography.

Because the mass was slowly enlarging and becoming more firm, early exploration was performed. Torsion of the left ovarian pedicle associated with a necrotic ovarian cyst was found. Salpingo-oophorectomy was performed.

Twelve previously reported cases of torsion of the ovary have been reviewed. Early surgical intervention is recommended to minimize the potential morbidity and mortality from complica-

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tions associated with the presence of an ovarian cyst in the neonate.

Case Report

A premature female infant, one of twins, was delivered by primary Cesarean section at 37 weeks of gestation to a 25-year-old mother, gravida 2 para O. Birth weight was 1,980 grams. No maternal complications had been reported in the prenatal period. The other twin was also a girl.

The patient's Apgar score was 6 at one minute and 8 at five minutes. There was no fetal distress. Vital signs were recorded as follows: temperature, 95.6°F; heart rate, 150/min; respiratory rate, 66/min; and blood pressure, 71/31 mm Hg. An initial arterial blood gas sample drawn at 15 minutes of age revealed the following: pH, 7.28; P_{CO_2}, 38.7 mm Hg; and P_{O_2} 92.6 mm Hg on room air. The hematocrit was 49%, and urinalysis was within normal limits.

Significant physical findings on the first day of life were limited to the abdomen, where an ovoid, well circumscribed mass measuring 5 × 5 cm was palpated on the left side of the abdomen, extending from the costal margin to the anterior superior iliac spine. The mass could be moved slightly toward the midline and did not appear to be tender. The infant did not pass meconium until 36 hours of age. Thereafter, normal meconium was passed, which was guaiac negative.

Initially, the mass was suspected of being renal in origin, and renal radionuclide scintigraphy was performed. The scan revealed prompt visualization of both kidneys and a large, avascular mass lateral and inferior to the left kidney, which appeared to be contiguous with the kidney, but not part of it. Ultrasonography showed a complex mass, anterior and inferior to the left kidney (Fig 1).

A barium enema showed persistent medial displacement of the descending colon, but no intrinsic abnormalities of the colon were obvious (Fig 2).

Contrast computed tomography disclosed a homogeneous mass occupying the entire left side of the abdomen. No clear cleavage plane could be delineated between the mass and the lateral abdominal wall or between the mass and the left kidney, raising the possibility of a renal cyst or a retroperitoneal tumor (Fig 3).

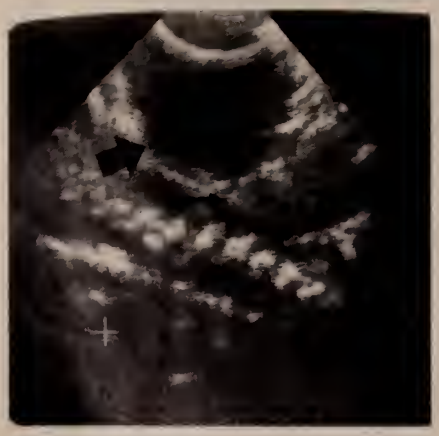

FIGURE 1. Real-time sonogram in longitudinal section. Small arrow points to left kidney. Large arrow points to predominantly hypoechoic mass anterior and inferior to the kidney.

FIGURE 2. Barium enema showing medial displacement of the descending colon suggesting extraperitoneal location of the mass.

Despite reliance on these findings, their individual interpretations did not lead to a definitive diagnosis, prolonging the preoperative evaluation.

A gynecological consultant did not feel any pelvic abnormalities, but adnexal disease could not be ruled out, since ovarian tumors or cysts in infants may rise up out of the true pelvis into the abdominal cavity. During the period of diagnostic evaluation, the mass became slightly larger, firmer, and more fixed in position than on initial examination. In view of the evolving nature of the clinical findings and the possibility of malignancy, exploratory surgery was performed on the eighth day of life.

The peritoneal cavity was entered through a left-sided transverse abdominal incision, dividing the left rectus muscle cephalad to the level of the umbilicus.

Upon entering the peritoneal cavity, a globular cystic mass 6 cm in diameter was found in the left upper quadrant just below the spleen. It was smooth-walled, violescent in color, and could easily be moved into the incision. The base of the mass was associated with the left fallopian tube, which had a "corkscrew-like" configuration, and was, in turn, continuous with the left cornual area of the uterus, which was being displaced upward, out of the pelvis. The descending colon was medial to the mass and adherent to the fallopian tube by a frond of fibro-fatty tissue stretching from the serosa of the bowel to the twisted tube. The right ovary and fallopian tube appeared normal on gross examination.

The mass and the twisted fallopian tube were resected together after ligation and division of the band attached to the serosa of the colon. The abdominal incision was closed in layers. The patient's postoperative course was uneventful.

On microscopic examination, the ovary was necrotic, with only a peripheral shell of connective tissue recognized. The fallopian tube contained a mass of blood and fibrin, surrounded by connective tissue with infiltration of inflammatory cells, granulation tissue, and calcification.

Discussion

The rarity of ovarian cysts in the neonate, especially those that have undergone torsion, presents an interesting and challenging diagnostic problem. A large proportion of neonatal abdominal masses are renal in origin,[1] but the true nature and diagnosis of the mass may not be discovered until laparotomy.

In the neonate, an ovarian cyst that undergoes torsion is extremely rare. A review of the literature shows that only 12 such cases have been reported previously (Table 1).

As cited in Karrer and Swenson,[2] Franque described the first case, noted in a stillborn in 1909. Longino and Martin[1] in 1958 and Karrer and Swenson[2] in 1961 reported successful surgical treatment of torsion of an ovarian cyst in the neonate.

In his 1965 review, Marshall[3] tabulated 23 cases of ovarian cyst in the neonate, of which only two were complicated by torsion. Cox et al[4] reported a case of ovarian cyst with torsion in a newborn which led to shock and death before the proposed surgical intervention could be initiated. Ahmed,[5] in reviewing the literature in 1971, found reports of 47 neonatal ovarian cysts. He added six cases to the literature, of which two were complicated by torsion. To this compendium, more recent case reports

FIGURE 3. Computerized tomography showing low density mass anterior to the left kidney (large arrow). Small arrow points to the left kidney opacified with contrast.

TABLE 1. Ovarian Cysts with Torsion in the Newborn

Source	Pathologic diagnosis	Comment
Franque, 1909	Simple cyst, torsion	Stillborn
Sun, 1951	Simple cyst, torsion	Stillborn
Longino, 1958	Cysts, torsion, hemorrhage	Oophorectomy
Karrer, 1961	Follicle cyst, torsion, gangrene	Oophorectomy
Boles, 1961	Follicle cyst, torsion	Oophorectomy
Hasse, 1962	Cyst, torsion	Oophorectomy
Cox, 1969	Cyst, torsion, hemorrhage	Autopsy finding
Ahmed, 1971	Cyst, torsion	Adherent to bowel; oophorectomy; postoperative death
Ahmed, 1971	Cyst, torsion, gangrene, rupture	Salpingo-oophorectomy
Tai, 1972	Cyst, torsion	Oophorectomy
Dieter, 1980	Cyst, torsion	Adherent to small bowel; salpingo-oophorectomy
Avni, 1983	Cyst, torsion, necrosis	Antenatal diagnosis by sonography; oophorectomy
Miller, 1984	Cyst, torsion, necrosis	Adherent to large bowel; salpingo-oophorectomy

by Tai,[6] Dieter et al,[7] and Avni et al[8] have been added. The patient described in this report represents the 13th such case.

The clinical presentation of an ovarian cyst in the neonate is commonly as an asymptomatic abdominal mass. The differential diagnosis must include hydronephrosis, renal cyst, urachal cyst, mesenteric cyst, intestinal duplication, Wilm's tumor, and neuroblastoma. An ovarian cyst may also present as an acute abdominal crisis in association with one of the reported complications, such as torsion, hemorrhage, rupture, intestinal obstruction, infarction, or incarceration within an inguinal hernia.

A renal origin for an unknown abdominal mass in a newborn must be considered first. Since intravenous pyelography in the newborn is falling into disfavor due to the poor concentration of contrast medium in the underdeveloped kidneys of the neonate, renal radionuclide scintigraphy is often used. It is a satisfactory, informative, and safe procedure.

Ultrasound is also a valuable diagnostic tool. Its use in the prenatal period now makes it possible to delineate a cystic abdominal mass in the fetus.[8] Computerized tomography is also a helpful diagnostic tool.

Interestingly, in two of the cases reported,[2,4] the presenting mass was palpable on the contralateral side of the abdomen from the involved ovary noted at laparotomy. A palpable mass in the mid-abdomen does not preclude ovarian origin, since the ovary in the newborn female is close to the general abdominal cavity, and the pedicle is long.[1,9]

Timely surgical intervention is still the best way to establish a diagnosis and to avoid the potential complications associated with an ovarian cyst.[4,5] Infarction of the ovary necessitates oophorectomy. If the fallopian tube is viable, it should be preserved, with consideration given to repositioning the fimbria in proximity to the contralateral ovary, to enhance future fertility.[10]

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Ocular myasthenia gravis and chronic inflammatory polyradiculoneuropathy

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Although myasthenia gravis has frequently been associated with autoimmune disorders,[1-4] it has only rarely been reported in association with other diseases of the nervous system.[5] Chronic inflammatory polyradiculoneuropathy, in contrast, has been commonly associated with systemic diseases,[6-7] but only rarely has it been linked to autoimmune phenomena[8-9] or to another neurologic illness. We recently evaluated a patient in whom clinical, laboratory, and electrophysiological studies were consistent with the temporal concurrence of ocular myasthenia gravis and chronic inflammatory polyradiculoneuropathy.

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Case Report

A 72-year-old man experienced progressive horizontal and vertical diplopia in November 1982. One month after these symptoms began he noted progressive bilateral

lower extremity weakness, most marked distally. Subsequently, a right foot drop developed. Initial evaluation included a temporal artery biopsy, computed tomographic brain scan, and edrophonium chloride test; the findings were unremarkable. His medical history was notable for chronic vitiligo, multinodular substernal goiter with normal thyroid function tests, and abnormal glucose tolerance without overt diabetes. There were no occupational exposures and no family history of neurological diseases.

The patient was admitted to the hospital in March 1983. A nonneurologic physical examination was remarkable for vitiligo and an enlarged multinodular thyroid gland with tracheal deviation. On neuro-ophthalmologic examination, the acuity was 20/30 in each eye with normal color vision and full tangent visual fields. The pupils were equal and reactive to light. The optic discs were normal with mild atherosclerotic changes in the retinal vessels. There was no exophthalmos. Bilateral ptosis was present with poor orbicularis oculi strength. The extraocular movements were limited in all fields of gaze. The right eye did not adduct past midline, and there was only 3–4 mm of horizontal motion and 6 mm of vertical movement. The left eye showed 2–3 mm of horizontal motion and 4 mm of vertical movement. Forced ductions revealed a mild, diffuse restrictive component, especially in abduction OU. The remainder of the cranial nerves were unremarkable. Muscle power testing was normal in the upper limbs. Power was graded at 4/5 (Medical Research Council Scale) throughout the left leg, and 4/5 in the right hip, knee, and ankle plantar flexors. A right foot drop was present, with 3/5 power in ankle dorsiflexion and eversion. The deep tendon reflexes were symmetric throughout and absent at the ankles. The plantar response was flexor bilaterally. A right steppage gait was present. The cerebellar and sensory examinations were unremarkable.

Intravenous edrophonium chloride, given in 2 mg increments every 15 seconds to a total dose of 10 mg, produced a marked improvement in extraocular movement without improving leg weakness.

Results of extensive blood tests to exclude metabolic, neoplastic, or rheumatologic disease were unremarkable. An oral glucose tolerance test revealed impaired glucose tolerance, with a fasting glucose of 126 mg/dL and a two-hour glucose of 182 mg/dL. The level of acetylcholine receptor antibody was 2.0 nanomoles/liter by radioimmunoassay (normal, 0–1 nmoles/L). A rectal biopsy was negative for amyloid. Subsequent mediastinal biopsy yielded only thyroid tissue, without thymomatous rests. The lumbar puncture showed normal opening pressure, with clear cerebrospinal fluid and no cells; the protein count was 128 mg/dL with a glucose level of 86 mg/dL and gammaglobulin level below 6%. Oligoclonal banding and cytology studies were negative. Computed tomographic studies of the brain, orbits, and lumbosacral spine were unremarkable. A contrast computed tomographic scan of the mediastinum was notable for a large substernal thyroid with a heterogeneous density and calcifications in the superior mediastinum.

Ocular electromyography revealed definite recruitment to edrophonium. Peripheral nerve conduction studies indicated slowing in all motor nerves in the lower extremities, ranging between 33.6 m/sec in the right tibial nerve to 34.2 m/sec in the right peroneal nerve. All sensory nerve potentials in the upper and lower limbs were of moderately diminished amplitudes and velocities, ranging from 3.0 ms in the right ulnar (amplitude, 16 microvolts) to 3.4 ms in the right superficial peroneal (amplitude, 8 microvolts). Electromyography found abnormal spontaneous activity in the paraspinal muscles of the L4–S1 dermatomes on the right and the L4–5 dermatomes on the left, with active denervation on the right. On repetitive stimulations of the right ulnar and spinal accessory nerves there was no decrementation, both before and after exercise. Right facial nerve stimulation produced a 24–34% decrement at 3 pulses per second, reproducible on many trials. Intravenous edrophonium chloride reduced the amount of decrementation to 18%.

Clinically, the patient's oculomoter deficits responded to pyridostigmine, with marked improvements in abduction, elevation, and depression, but with limited improvement in adduction. There was no improvement in leg weakness.

Readmission during July 1983 was prompted by a gradual exacerbation of oculomotor symptoms following the tapering of pyridostigmine. A neuro-ophthalmologic examination disclosed bilateral ptosis with almost complete ophthalmoplegia. Mild orbicularis oculi weakness was present. The limb weakness was unchanged, and mild atrophy of the right tibialis anterior and peroneal muscles was noted. The deep tendon reflexes were normal in the arms, hyporeflexic at the knees, and absent at the ankles. The plantar response was flexor. A sensory examination revealed mild decrements in vibratory and pain sensation in the hands and below the knees, with preservation of touch and proprioception. Intravenous edrophonium chloride produced marked improvement in the oculomotor deficits, ptosis, and facial weakness.

Repeat clinical and radiological exams for systemic illness and malignancy were unrevealing. The acetylcholine receptor antibody titer was at the upper limit of normal. A repeat cerebrospinal fluid examination was normal, with a protein count of 35 mg/dL. Nerve conduction studies again revealed a sensorimotor polyneuropathy with prominent demyelinating features, most severe in the legs and unchanged in magnitude from the prior examination. Electromyography demonstrated less evident active denervation in the lumbar distribution on the right than was found previously. A sural nerve biopsy was attempted but was not achieved.

The patient was treated with pyridostigmine, 480 mg/day in divided dosages, and prednisone, 100 mg/day. There was prompt resolution of the ocular deficits. Within a six-week period, there was complete improvement of the leg weakness and right foot drop. The patient has maintained normal neurologic function during a two-year follow-up period, but has not been able to tolerate complete prednisone withdrawal due to recrudescence of the ocular myasthenia gravis at lower dosages.

Discussion

This patient demonstrated characteristics of myasthenia gravis by the unequivocal response of his oculomotor deficits to anticholinesterase therapy and by the significant amplitude decrement to supramaximal repetitive stimulations in the facial nerve.[10] The marginal elevation in acetylcholine receptor antibody found in this patient is often a feature of the oculomotor variety of myasthenia gravis. Sera from patients with ocular myasthenia gravis react better with receptors from ocular or normal skeletal muscle than with receptors from the denervated skeletal muscle which is used in most assays.[11] This patient's clinical features conform to those of a major subgroup of patients with myasthenia gravis described by Compston et al.[12] This population comprises predominantly men over 40 years of age with low acetylcholine receptor antibody titers and without evident thymoma. The Human Leukocyte Antigen groups A3, B7, and DRW2 are most often present, and one third of these patients have other autoimmune diseases. The initial negative response to intravenous edrophonium chloride may have been the result of excessively rapid administration, resulting in a paradoxical suppression of the acetylcholine receptor and a false negative outcome.[25]

In addition, this patient's symptoms fulfilled the criteria for a diagnosis of chronic inflammatory polyradiculoneuropathy[6,7,13]: presence of an ingravescent sensorimotor polyneuropathy affecting the lower extremities, reaching a nadir of disability within a 12-month period; slowing of nerve conduction velocities; elevated cerebrospinal fluid protein level; and absence of significant systemic illness or toxic exposure. The temporal relationship between the application of high dose steroid therapy and the complete resolution of limb weakness is also compatible with this diagnosis.[13]

Reported associations between myasthenia gravis and nervous system disorders in general, as well as neuropathies in particular, appear only sporad-

ically in the literature.[5] Goldfarb[14] described a young man in whom unilateral intercostal neuritis rapidly evolved to diffuse weakness and areflexia with a normal cerebrospinal fluid profile, and in whom edrophonium chloride yielded a dramatic reversal of motor deficits. Brust and colleagues[5] reported on a 20-year-old man in whom spastic paraparesis developed, with elevated cerebrospinal fluid protein levels, in association with a febrile illness at age four. An oculomotor deficit mimicking chronic progressive external ophthalmoplegia began at age 11 and progressed during his teenage years. Neurological evaluation revealed an external ophthalmoplegia, spastic paraparesis with Babinski signs, and peripheral neuropathy. Electrical studies demonstrated chronic sensorimotor polyneuropathy with both demyelinating and denervating features, most pronounced in the legs, along with a defect in neuromuscular transmission consistent with ocular myasthenia gravis. The external ophthalmoplegia improved with anticholinesterase agents, without affecting limb weakness. The authors concluded that other patients with chronic progressive external ophthalmoplegia with associated neurologic signs may well have had occult myasthenia gravis. Bourouresques and coworkers[15] reported on a 42-year-old woman with classical myasthenia gravis and a benign thymoma in whom an acute ascending polyradiculoneuritis (Guillain-Barré syndrome) developed approximately nine months after the myasthenia gravis was diagnosed. A muscle biopsy demonstrated neurogenic atrophy and mononuclear infiltration in the interstitial tissues. Immunofluorescence revealed immunoglobulin G deposits in the perineurium and muscular interstitium. The polyradiculoneuritis rapidly improved, while the myasthenia-gravis-related deficits persisted. An autoimmune disturbance common to both diseases was postulated. Two cases of acute polyradiculoneuritis combined with myasthenia gravis were documented by Regev et al.[16] A 60-year-old woman had acute polyradiculoneuropathy confined to the legs, with absent deep tendon reflexes and delayed conduction velocities. Ptosis, exertional dyspnea, and diffuse weakness developed two weeks later; these symptoms were responsive to edrophonium. Elevated titers of acetylcholine receptor antibodies were present. A 29-year old woman with cranial polyneuritis also developed ptosis, dyspnea, and diffuse weakness after a two-week period, along with abnormally elevated acetylcholine receptor antibodies. This patient also improved with anticholinesterase treatment. The clinical evolution of these patients led the authors to suggest that the presynaptic immune response, directed initially at a peripheral nerve antigen, may have altered the postsynaptic acetylcholine receptor, provoking an autoimmune response to the receptor. Bogousslavsky et al[17] described a 54-year-old man with a myasthenic syndrome and malignant thymoma in whom sensorimotor polyneuropathy, encephalopathy, and dysautonomia developed over the five-month period prior to his death. Electrophysiological studies were consistent with diffuse demyelinating and denervating polyneuropathy. Repetitive nerve stimulation studies did not demonstrate decrementation. The cerebrospinal fluid protein level was remarkable for albumino-cytologic dissociation and an elevated immunoglobulin G index. There was an elevated acetylcholine receptor antibody titer in both the serum and cerebrospinal fluid. Anti-skeletal muscle antibodies were also present in the serum. Necropsy revealed an invasive thymoma and diffuse cortical gliosis. The spinal cord and nerve roots were normal, and moderate interstitial fibrosis was observed in the peripheral nerves. Muscle infiltration by monocytic lymphocytes was present. A diagnosis of myasthenia gravis was made on the basis of these lymphorrhages and the elevated acetylcholine receptor antibodies in the serum. These investigators attributed the multiple neurologic derangements to a cholinergic dysfunction acting both centrally and peripherally.

Any hypothesis that would purport to account for the temporal concurrence of myasthenia gravis and chronic inflammatory polyradiculoneuropathy must address two separate questions: What disturbances in immune regulation, at both the cellular and humoral levels, are common to both diseases? What features of the immune disturbance and the target tissue antigens account for the infrequency with which myasthenia gravis and neuropathies occur together?

At present, answers to these questions are speculative. Myasthenia gravis is associated with a humorally mediated and complement dependent destruction of acetylcholine receptors on skeletal muscle; phagocytosis of motor endplates by macrophages via immune ligands probably serves as an effector mechanism.[2,3,18,19] Cell-mediated immunity to the acetylcholine receptor has been detected by lymphocyte stimulation and macrophage inhibition assays and typically occurs in elderly patients.[20] But this immunity is not felt to play a major role in the pathogenesis of the disease.[21] Immunologic studies of patients with chronic inflammatory polyradiculoneuropathy have detected linear immunoglobulin M deposits without complement in sural nerve specimens,[22] antibodies to axonal and to myelin components,[9] and perineural infiltration by lymphocytes and active demyelination by antibody-directed macrophages.[23] The major antigen in chronic inflammatory polyradiculoneuropathy is suspected to involve a plasmalemmal carbohydrate moiety which elicits a persistent thymus-independent immunoglobulin M response.[13] Cell-mediated responses to both central and peripheral nerve myelin basic protein have been detected in patients with chronic inflammatory polyradiculoneuropathy, but their role is uncertain.[24] Thus, although humoral factors appear to play a role in both diseases, the reasons for their origins and diversity are obscure. Recognition of areas of overlap and dissimilarity between myasthenia gravis and chronic inflammatory polyradiculoneuropathy is important when determining appropriate therapy.

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Listeria meningitis

Report of two cases

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Two cases of *Listeria monocytogenes* meningitis in otherwise healthy individuals are described to serve as a reminder that the non-immunocompromised host is also susceptible to this disease.

CASE REPORT

Case 1. A 68-year-old man sought treatment for fever, weakness, dizziness, inability to eat or stand, confusion, and decreasing memory. The funduscopic examination was normal, but his neck was moderately rigid. The Babinski sign was bilaterally equivocal. Cerebellar function could not be adequately assessed, as the patient could neither stand nor follow commands. The peripheral blood leukocyte count was 11,400/dL with 71% segmented neutrophils and 6% non-segmented neutrophils, 17% lymphocytes, and 6% monocytes. A chest roentgenogram and computerized tomographic (CT) scan of the head (with and without contrast) were within normal limits. A lumbar puncture revealed the following: 1,300 leukocytes with 95% segmented neutrophils and 5% monocytes, and 770 erythrocytes; glucose, 45 mg/dL; protein, 228 mg/dL, and chloride, 118 mEq/L. A Gram's stain showed numerous polymorphonuclear leukocytes with gram-positive rods, later identified as *Listeria monocytogenes*. Antimicrobial therapy with ampicillin and gentamicin resulted in noticeable improvement in alertness and responsiveness over the next several days. Meningeal signs were absent. One month after discharge, the patient was fully ambulatory with a steady though wide-based gait, but without residual memory impairment.

Case 2. A 58-year-old man sought treatment for throbbing frontal and occipital headaches, insomnia, neck stiffness, and photophobia of two days' duration. Meningeal signs were not present, but he had an inappropriate affect. The peripheral blood count included a leukocyte count of 9,600/dL with 80% segmented neutrophils and 5% non-segmented neutrophils, 4% lymphocytes, and 11% monocytes. Chest and skull radiographs and a CT scan of the head were normal. A lumbar puncture revealed the following: opening pressure 16 cm water; five erythrocytes; and 84 leukocytes with 36% segmented neutrophils, and 64% non-segmented neutrophils. The cerebrospinal fluid (CSF) protein count was 80 mg/dL. *Listeria monocytogenes* was cultured from the CSF fluid. Treatment with intravenous penicillin for 15 days produced full resolution of signs and symptoms.

DISCUSSION

Listeria monocytogenes is a short, facultative, and anaerobic gram-positive rod. *Listeria* infections can present in a variety of ways. In the fetus or newborn, the chief clinical syndromes are stillbirth, early-onset septicemic illness that may mimic hyaline membrane disease, and late-onset meningitis similar to that due to group B streptococcus.[1] In adults, the syndromes caused by *L monocytogenes* include meningitis, non-meningitic infection of the central nervous system (CNS), primary bacteremia, and endocarditis.[2]

The organism is found worldwide.[1] In humans, it can be associated with overt disease or an asymptomatic carrier state. Originally, animals were thought to be the main source of *Listeria* infections in humans.[3] Outbreaks of listeriosis have been traced to contaminated food, such as cabbage fertilized with contaminated sheep manure, and contaminated pasteurized milk. A recent outbreak of 86 cases of listeriosis was traced to contaminated Mexican-style cheese in Los Angeles and Orange Counties, California.[4]

In a review of listeriosis in adults from 1968 to 1978, Nieman and Lorbar[2] found that infections in adults were increasing in frequency, due to a combination of factors, including the extensive use of cancer chemotherapy and renal transplantation resulting in increased numbers of susceptible patients. Risk groups include elderly adults, neonates, and those suffering from chronic diseases in which T-cell function is compromised, such as alcoholism, diabetes mellitus, and collagen vascular diseases.[2]

Meningitis is the most common adult presentation of listeriosis, particularly in the elderly. In one series of 53 cases of *Listeria* meningitis reported between

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1972 and 1979, 41 patients were adults over 50 years of age.[5] Though generally acute in onset, *Listeria* meningitis may develop gradually over days or longer. Unlike other forms of bacterial meningitis, nuchal rigidity may be absent in up to 20% of cases, and movement disorders such as tremors, ataxia, myoclonus, seizures, and fluctuating mental status occur more commonly in *Listeria* meningitis.[2]

Distinctive laboratory features of *Listeria* meningitis include the absence of a low glucose level in the CSF and a lack of a predominance of neutrophils in the CSF in many cases. The level of CSF protein (25–1,000 mg/dL) tends to be higher in patients who die. Blood cultures are positive in about 75% of patients, and fever is nearly universal. The non-meningitic CNS forms of infection are less common and range from localized abscesses and cerebritis to diffuse encephalitis. Recently, two cases of non-meningitic *Listeria* rhombencephalitis were reported.[6]

The two cases reported here represent *Listeria* meningitis in otherwise healthy adults. These cases and the reviewed literature support the belief that while *Listeria* meningitis must always be considered in the immunosuppressed patient, this diagnostic possibility should not be overlooked in the healthy population. Finally, physicians should be aware of the increasing incidence, changing epidemiology, and clinical syndromes of *Listeria monocytogenes* infection in order to make an earlier diagnosis and institute appropriate therapy.

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Maternal and fetal mortality in acquired immunodeficiency syndrome

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Since the initial report by the Centers for Disease Control (CDC) on acquired immunodeficiency syndrome (AIDS) in homosexual men,[1] the syndrome has been found in other social and ethnic groups, as well as in various geographic areas. As of January 1986, 16,458 cases had been reported in the United States.[2] As of September 1985, 1,573 cases had been reported from collaborating European countries.[3] Most of the reported U.S. and European cases were among male homosexuals or bisexuals, while the other risk groups included intravenous drug abusers, hemophiliacs, transfusion recipients, and heterosexual contacts. Approximately 90% of the cases have been reported in the 20–49-year age group, and 7% of reported cases have been among women.[2,3] Recent reports of AIDS during pregnancy and among newborns and children raise concerns about transmission in utero.[4,5]

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We present the case of an AIDS-related maternal mortality during pregnancy. Similarities between the immunology of pregnancy and AIDS are outlined. Also discussed are the hazards of current available therapy for the fetus and advice for the management of the pregnant patient with AIDS.

Case Report

A 33-year-old woman, gravida 4, para 2, was admitted to Bellevue Hospital at 26 weeks' gestation, complaining of several hours of uterine contractions without rupture of membranes or bleeding. She also complained of nonproductive cough, general weakness, malaise, and shortness of breath of two weeks' duration. She had had only one prenatal visit during this pregnancy. The prenatal data revealed a nonreactive VDRL test, a negative purified protein derivative (PPD) skin test, and a negative gonorrhea culture from the cervix. The patient was an intravenous drug abuser of seven years' duration and was currently on methadone, 15 mg daily. Her last heroin injection had been two months prior to admission. She also had a two-year history of severe mucocutaneous candidiasis.

The patient had been a prison inmate for the last four months. In 1982, her female roommate of two years' duration was diagnosed as having AIDS and expired several months later. The patient denied sexual contact or needle sharing with this individual. However, she admitted to having had multiple sexual partners, with no knowledge of sexual contact with a partner who had AIDS.

Her obstetrical history included two vaginal deliveries of normal infants in 1976 and 1981, without complications. The children are alive and well. She denied a history of pelvic inflammatory disease or sexually transmitted diseases.

Physical examination revealed a healthy appearing woman in mild respiratory distress. Her blood pressure was 120/70 mm Hg; pulse rate, 90/min; respiratory rate, 26/min; and temperature, 101.6° F. Oral candidiasis was present. Small diffuse, nontender cervical and supraclavicular lymphadenopathy was noted bilaterally. Auscultation of the lungs revealed coarse rhonchi bilaterally. An abdominal examination disclosed a gravid uterus of approximately 24 weeks' size and palpable contractions every two minutes. No enlargement of other viscera was noted. Old needle marks were noted on the extremities. A neurological exami-

nation was within normal limits. On pelvic examination, the cervix was 50% effaced and 1 cm dilated. Vulvovaginal candidiasis was present.

Laboratory studies revealed a hemoglobin of 9.5 g/dL; hematocrit, 28.4%; white blood cell count, 11,800/μL with 14% lymphocytes. Renal and liver function tests were normal for pregnancy. Initial arterial blood gas data yielded a pH of 7.49, a P_{CO_2} of 28 mm Hg, and a P_{O_2} of 46 mm Hg. Urinalysis, cultures, and sensitivity tests were negative. Blood cultures were also negative. A chest radiograph revealed bilateral interstitial infiltrates (Fig. 1). A real time ultrasound examination revealed a live fetus of 24 weeks' gestation.

Initial therapy included supplemental inspired oxygen, trimethoprim/sulfamethoxasole, erythromycin, and oral nystatin. The patient was also placed on intravenous ritodrine for tocolysis. A transbronchial biopsy was performed on the second hospital day. *Pneumocystis carinii* organisms were identified on Grocot's silver stain. Two days later, increased oxygen supplementation was given to maintain an arterial P_{O_2} of greater than 70 mm Hg. The patient was transferred to the intensive care unit and pentamidine isethionate therapy was started.

Despite intravenous ritodrine therapy, the patient continued to have uterine contractions. Amniotic fluid cultures were all negative, as were smears and cultures for acid-fast bacilli. Testing for cryptococcal antigen proved negative. The pregnancy continued untreated as there were no cervical changes to suggest the onset of labor. On the seventh hospital day, there was a further deterioration of the patient's respiratory status. Endotracheal intubation and assisted mechanical ventilation were required. At this time, the fetal heart rate was 140/min. The patient sustained two cardiopulmonary arrests requiring hemodynamic and ventilatory support. Despite aggressive management with vasopressor agents, the patient died on the eighth hospital day. Shortly before her death, fetal demise was confirmed by real time ultrasound.

Postmortem examination of the mother and fetus was performed. In addition to routine histologic staining of fetal and maternal tissues—specifically the uterine implantation site and the placenta—selected blocks of tissue were stained with Gram's, Grocot, Mucicarmine, and periodic acid-Schiff stains. *Pneumocystis carinii* was found only in the maternal lungs. No other infectious agents were noted.

Discussion

The acquired immunodeficiency syndrome is currently epidemic in various geographic areas of the world. Of concern is the growing number of heterosexuals, newborns, and infants with AIDS or an AIDS-like syndrome without identifiable risk factors. Both in the US and in Europe, the number of new cases reported every year continues to increase. Between June 1, 1981 and January 13, 1986, 16,458 cases had been reported in the US. The absolute number of AIDS cases in women continues to increase. Women currently represent approximately 7% of all reported cases. More cases among pregnant women can be expected since approximately 90% of all AIDS cases occur among those 20–49 years of age, the prime reproductive age group.[2]

FIGURE 1. Chest film depicting bilateral interstitial infiltrates.

To our knowledge, this case represents the first reported maternal death during pregnancy due to AIDS. In 1984, Jensen et al[6] reported on a Haitian woman who died of *Pneumocystis carinii* pneumonia on the 11th postpartum day. It is important to note the resulting morbidity among pregnant patients, including the patient described in this report. The nature of the mother's opportunistic infection may only partially account for the fatal course, whereas pregnancy itself could play a significant role. *Pneumocystis carinii* is by far the most common opportunistic infection seen in patients with AIDS, accounting for approximately 62% of all AIDS associated infections.[7] A National Heart, Lung, and Blood Institute workshop reported that, of 1,067 patients with AIDS, 441 had pulmonary disorders, of which 373 (70%) were due to *Pneumocystis carinii* pneumonia, either alone or coexisting with one or more other infections. Eighty-six percent of patients who required endotracheal intubation and mechanical ventilation, and 89% of those who were switched to pentamidine because of trimethoprim/sulfamethoxazole resistance, subsequently died.[7] The patient described in this report features many of the clinical aspects associated with a poor outcome.

Clinical and laboratory studies indicate that maternal cell-mediated immunity is depressed during pregnancy.[8] In many ways, the immunologic changes during pregnancy are similar to those described in patients with AIDS. In both conditions, there is a depressed immune system, with some lymphocyte subsets not fully functional. In AIDS, there is a reversal of helper-to-suppressor-cell ratios (T4/T8) due to a profound depression of the number of T4 helper cells. The T4/T8 ratio in pregnancy is usually reported to be slightly depressed.[9] The histopathologic changes observed in the thymus, lymph tissue, and spleens of patients with AIDS are suggestive of similar, but milder, changes seen in pregnancy.[10]

The immunological changes in both pregnancy and AIDS may be additive, causing suppression of the immune system to an irreversibly nonfunctional state. Theoretically, this may accelerate maternal death in patients with AIDS, who in the nonpregnant state already have an exceptionally high mortality rate of at least 60% and possibly higher.

Although the HTLV-III/LAV virus was not identified in fetal tissues in the patient reported here, available data suggest that the virus is transmitted from infected mothers to their fetuses during pregnancy or during labor and delivery.[11] In the postnatal period, blood transfusions and breast feeding have been implicated as possible modes of transmission.[12] Fifty-nine percent of children with AIDS are reported to have died as of January 1986.[2]

Little attention has been given to the potential hazards to the fetus of current available therapy. The patient in this report had been treated initially with trimethoprim/sulfamethoxazole. Then pentamidine isethionate was added. The use of sulfonamides in pregnancy has been associated with kernicterus of the newborn.[13] Although there is no evidence that trimethoprim is harmful, other folate antagonists are known to be teratogenic. Pentamidine isethionate has been associated with severe hypotension, hypoglycemia, hyperglycemia, cardiac arrhythmia, leukopenia, and renal and hepatic dysfunction in the adult mother.[14] Little is known about the effects of this drug on the fetus, since current experience with pregnant women is limited. Pentamidine appears to interfere with the synthesis of RNA and DNA by protozoa such as *Pneumocystis carinii*. Difluoromethyl ornithine (DFMO) is another experimental alter-

native to pentamidine and to trimethoprim/sulfamethoxazole. This antiprotozoal agent inhibits the activity of ornithine decarboxylase, which is an essential enzyme for cell division.[15] The effect of these drugs on the fetus, although not known, would appear unfavorable.

In conclusion, AIDS during pregnancy will become more common, and will be seen most often in tertiary care centers in large cities. Obstetricians and specialists in maternal-fetal medicine should become familiar with AIDS in pregnancy. Given the present state of knowledge, the potential risks to both mother and fetus should be thoroughly discussed with the patient or parents early in pregnancy. Delaying pregnancy in high risk groups is advisable until additional information is available on the risk of perinatal transmission of the virus. Until then, the spread of the AIDS virus may lead to an increase in maternal and infant mortality in the United States and abroad.

Acknowledgment. The authors thank Drs Alvin Friedman-Kien and Bradley Bigelow for their helpful comments on the manuscript.

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FROM THE LIBRARY

ON THE USE OF ERGOT IN THE TREATMENT OF PURPURA

The inefficiency of the commonly-employed and recommended treatment of purpura, in its various forms, must have impressed every one who has come much in contact with the disease, and caused them irresistibly to wish that something more definite was known in regard to its etiology, pathology and therapeutics, and to long for some remedy which would really exercise a controlling power over the disease. Without attempting to enter into a description of purpura, nor to throw any new light upon its etiology or pathology, I desire to call very serious attention to the great value of ergot in this disease. Although this was announced by Horroch eight years ago, and its truth confirmed soon after by Bauer, and although this treatment has been reported on most favorably, in isolated cases, within the last few years, ergot is yet far from being recognized as being an efficient remedy in purpura; most of the textbooks on cutaneous diseases and general medicine not mentioning it at all, others but briefly. . . .

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(*Trans Med Soc State NY* 1876; 165)

This section is designed to offer rapid publication (usually within 1–3 months) of new clinical, epidemiologic, and laboratory observations, as well as of comments on articles published in the Journal *or on any topic related to the role of the physician. Letters should be typed double-spaced and should include the professional affiliation, highest academic degree, address, and signature of each author. Preference is given to letters not exceeding 450 words. All letters are personally reviewed and acknowledged by the Editor. Address correspondence to Editor,* New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042.*

AIDS in Third World countries

TO THE EDITOR: I am writing this letter in response to Dr DeHovitz's commentary, "A perspective on the heterosexual transmission of the acquired immunodeficiency syndrome (1986; 86:117–118).

Dr DeHovitz puts forth the notion that a possible reason why there is such a high incidence of AIDS in heterosexual males in Haiti and in Central Africa is because of the high incidence of sexually transmitted disease in these areas. He states that such frequent infections cause breaks in the skin of the penis, creating a portal of entry for the HTLV-III/LAV virus during coitus in which there is contact with infected vaginal secretions.

It has been observed that AIDS is primarily a heterosexual disease in Central Africa and in Haiti.[1,2] It has also been observed that the men in whom the HTLV-III/LAV virus has been found have had contact with female prostitutes.

To my knowledge, homosexuality is not prevalent in Central Africa, nor is it prevalent in Haiti. It is now clear that homosexuals from the US traveled in the late 1970s and early 1980s to Haiti and to Brazil for the purpose of engaging in sexual activities with young black men. In my view, this is how the disease found its way to both Haiti and Brazil.

With regard to the situation in Central Africa, it is not quite clear how the problem evolved. There is, however, evidence that unsterile injection equipment may play a role. This is one way that the disease can be transmitted. There is also a high incidence of HTLV-III/LAV in blood products that are used in Central Africa. That is another possible means of transmission.

The notion that the AIDS virus had its genesis from Africa is a controversial topic. In my opinion, the data are not at all convincing as to where the virus originated.

It is my opinion that because the majority of men from Central Africa and Haiti are not circumcised, they constantly develop balanitis as a result of the heat and other problems, leading to breakage of the skin. This leads to chronic infections such as phimosis and paraphimosis. In this setting, there is frequent mini-ulceration of the foreskin of the penis. This represents an easy portal of entry for the virus during coitus with, let us say, an infected prostitute. Another possibility arises because the women in that part of the world do not shave the pubis. Thus there is the possibility of mini-lacerations occurring during coitus as the foreskin comes into contact with pubic hair. This is another possible portal of entry for the virus. This, to me, seems a more plausible explanation for female-to-male transmission in Central Africa and Haiti.

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In reply. Although AIDS appears to be primarily a heterosexual disease in Central Africa, there is no doubt that homosexuality has played an important role in the transmission of AIDS in Haiti. Indeed, studies by our group at Cornell University in collaboration with the Haitian Study Group on Kaposi's Sarcoma and Opportunistic Infections (GHESKIO) revealed that more than one third of males with AIDS in Haiti had a history of a homosexual encounter.[1] The role that unsterile needles and syringes play in the transmission of this disease has not yet been clarified. The need for further studies regarding transmission of HTLV-III/LAV by unsterile injections was addressed in the accompanying editorial by Dr Imperato.[2] Dr Alcena raises an interesting point about the role that phimosis and paraphimosis in uncircumcised men may play in the transmission of the AIDS virus. This may indeed lead to a lymphocyte response, increasing the ease of virus inoculation from HTLV-III/LAV infected individuals. The disruption of mucosal integrity might also be a contributing factor. However, male circumcision is widespread in sub-Sahara Africa and is performed in many of the areas where AIDS has been identified.[3] As with the investigation of any postulated risk factor for AIDS, well controlled epidemiologic studies should also address the issue of male circumcision.

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AIDS and the adult respiratory distress syndrome

TO THE EDITOR: The article entitled "Disseminated cryptococcosis presenting as the adult respiratory syndrome" (1985, 85:704–706) represents a poor documentation of both the adult respiratory distress syndrome (ARDS) and the acquired immune deficiency syndrome (AIDS).[1]

The authors describe a 32-year-old male who was admitted to the hospital with what "appeared" to be AIDS. The patient developed respiratory distress documented only by arterial blood gases and some ill defined infiltrates on chest radiograph. His sputum smear was found to have no organisms, and was negative for acid fast bacilli. An open lung biopsy demonstrated bud-

ding *Cryptococcus neoformans*, and subsequent to this finding, all cultures of blood, sputum, urine, spinal fluid, pleural fluid, and lung tissue were found to be positive for this organism. The patient was also found to have high titers of cryptococcal antigen in the cerebrospinal fluid and in the blood.

The adult respiratory distress syndrome[2] is a well defined clinical entity. In order to meet the criteria for ARDS, one must show noncardiogenic pulmonary edema by demonstrating a normal range of left heart or pulmonary capillary wedge pressures, severe hypoxemia unresponsive to high concentrations of oxygen, intrapulmonary shunting, and stiffness of the lungs by measuring overall compliance of less than 50 cc/cm H_2O. Dead space ventilation may also be increased. None of these criteria are documented in this case report.

The statement "There is reason to believe he also had AIDS" is again poorly documented. The mere fact that the patient came from Haiti is not enough evidence that he had AIDS. This is akin to saying that a patient has Tay-Sach's disease because he is Jewish, or has "Kuru" because he came from Papua New Guinea.[3]

It would have been better to have shown that the patient met the World Health Organization's criteria for AIDS. The patient was not described as being gay or as having Kaposi's sarcoma, which is present in approximately 30% of cases. No abnormalities of T4 lymphocyte subsets were demonstrated, nor was there evidence of isolation of the etiologic retrovirus. One might also question why the patient was placed on the potentially hepatotoxic regimen of isoniazid, rifampin, and streptomycin in the face of a negative sputum acid fast smear.

Finally, in our own experience with approximately 55 cases of AIDS in a community teaching hospital, we have had to resort to open lung biopsy only once, having made the diagnosis of specific infection by bronchoscopy and transbronchial biopsy in all the other cases. It would be interesting to the readers to know if this was considered.

In summary, a stricter peer review of this case report might have made it a more scientifically valid study.

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In reply. We appreciate Dr Vevaina's comments regarding our case report and welcome the opportunity to respond to the points made in his letter.

This patient did meet the criteria for a form of adult respiratory distress syndrome (ARDS). He presented with a rapidly progressive, catastrophic respiratory illness requiring assisted mechanical ventilation. The chest film revealed characteristic extensive and relatively symmetrical bilateral infiltrative abnormalities. We referred in our case report to the patient's severe gas exchange abnormality; he required an F_IO_2 of 0.50 via a mechanical ventilator to maintain an arterial PO_2 of greater than 60 mm Hg. Although we did not include the data in the original report, the patient also had a very low lung compliance—ie, in the range of 15–20 cc/cm H_2O. Finally, we agree that right heart (Swan-Ganz) catheterization is very often important and helpful in patient management. However, this procedure is certainly not always necessary for the diagnosis of ARDS. In this particular case, the patient was a young man with no prior history of or risk factors for cardiac disease; there were no physical findings or electrocardiographic abnormalities to suggest a cardiac problem; radiographically, the cardiac silhouette remained within normal limits; and, furthermore, at postmortem examination there was no abnormality of the cardiovascular system to suggest that cardiogenic factors had been contributory.

In addition, this patient also met accepted criteria for the case definition of AIDS.[1] Disseminated cryptococcosis is generally accepted to be an opportunistic infection of immunocompromised individuals, and it is one of the principal opportunistic infections associated with AIDS.[2] This patient had not received any immunosuppressive medication and there was no evidence clinically or on postmortem examination to suggest an immunologic deficit other than AIDS. We referred in the report to the patient's history of diarrhea and his presentation with oral thrush and diffuse lymphadenopathy, all of which are additional findings to suggest AIDS. We agree that other than his Haitian background the patient had no acknowledged risk factor for AIDS. However, we cited references[3,4] documenting the occurrence of AIDS in Haitian individuals without more common risk factors (eg, homosexuality, drug abuse, blood transfusions). A more recent study[5] continues to confirm an unexplained increased risk of AIDS among Haitians. The immunologic and virologic studies mentioned by Dr Vevaina were not available in 1981 when this patient was managed.

Next, we would like to point out that miliary tuberculosis was initially a distinct possibility in the differential diagnosis of this patient's illness. Tuberculosis is endemic in Haiti and has proven to be a significant clinical problem among recent Haitian immigrants.[6] Also, miliary tuberculosis is well established as a lethal but potentially treatable cause of respiratory failure and ARDS.[7–9] In cases in which miliary tuberculosis is a diagnostic possibility, it is recommended that chemotherapy be initiated immediately on an empirical basis pending definitive diagnosis. Sputum AFB smears by themselves are not particularly sensitive in the diagnosis of miliary tuberculosis.[10–11] In one large reported series, sputum AFB smears were positive in slightly less than one third of the cases.[11] Given this background, we felt that the initial use of tuberculosis chemotherapy was prudent and appropriate. The potential short term risk of hepatotoxicity in a young patient with no obvious underlying liver disease was negligible and the potential benefits, had we been correct, could have been lifesaving.

Finally, we would like to address the question of the open lung biopsy in this case. It was thought clinically necessary to obtain a lung tissue specimen for diagnosis. For patients receiving positive pressure ventilation, there is a significant risk of tension pneumothorax due to transbronchial lung biopsy. Mechanical ventilation has even been considered as a possible contraindication to the use of such biopsies.[12] Thus, for patients receiving mechanical ventilation, we routinely perform fiberoptic bronchoscopy to obtain bronchial washings and bronchoalveolar lavage, but we opt for an open lung biopsy when a tissue diagnosis is required.

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FROM THE LIBRARY

ACUTE INFECTIOUS MONONUCLEOSIS
Report of a Case with 42,000 Leukocytes

. . . Dr. A. M., age 35, a German biochemist, came to the Presbyterian Hospital complaining of drowsiness, muscle pains, fever and headache, for three days. These symptoms had been preceded by a sore throat for two weeks. He felt that "something must be wrong" as he found it impossible to work. He coughed but raised no sputum. . . . On admission his temperature was 101.2, pulse, eight-four, respirations twenty, blood pressure 112/70. . . .

The first blood count showed 32,000 white cells with eighty per cent lymphocytes. A day or two after admission the blood picture was: Hgb one hundred per cent (100% = 14.9 gm. Hgb.); r.b.c. 5,200,000; w.b.c. 30,200; Neut. ten per cent (0-1-9); lymph. forty-one per cent; abnormal lymph. twenty-six per cent; mono. eight per cent; smudges fifteen per cent. The numerous abnormal lymphocytes and monocytes made an impressive picture but the absence of embryonal forms seemed to preclude leukemia. Many of the lymphocytes came in the class described by Downey as "leukocytoid." With hemoglobin and red cells normal we immediately thought of mononucleosis; this was confirmed by the agglutination of sheep red cells by the serum dilution of 1:128.

The Wassermann test was negative. In the throat culture streptococcus viridans predominated and no hemolytic organisms were seen. The temperature, as shown by the chart, continued to rise, and on the fifth day in the hospital reached 104.4. At this time the white blood cells were 42,000. We had never seen anyone so sick with mononucleosis and wondered if we had erred in our diagnosis. Should we expect any complications? Acute nephritis has been reported, but the urine never showed more than a trace of albumin and no casts were found. The temperature remained above 104 for a few hours and the next day, to our relief, reached only 103 and, as shown by the chart, came down steadily. The white cells fell rapidly with little change in differential count. The reduction in leukocytes roughly paralleled the drop in temperature.

The patient remained in the hospital for 20 days and made an uneventful recovery.

When seen three months after discharge he looked perfectly well with no nodes or spleen palpable; the blood count at that time was w.b.c. 10,000; neut. 53; eos. 12; baso. 1; lymph. 30; monos. 4.

It is hard to account for the presence of twelve per cent eosinophiles. So many are, I think, unusual after an attack of mononucleosis. We have no records that go over six per cent. This count was checked in a month and the differential remained practically the same except that the eosinophiles had dropped to six per cent. The rise in eosinophiles is hard to explain but at least it appears to have been only temporary. . . .

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(*NY State J Med* 1935; 35:908-909)

CANCER RISKS AND PREVENTION

Edited by M. P. Vessey, MD, and Muir Gray, MD. 301 pp, illustrated. New York, Oxford University Press, 1985. $29.95 (hardcover)

Sir Richard Doll learned epidemiology the old fashioned way: through experience. Yet Sir Richard is the very model of a modern epidemiologist; he continues to conduct important studies that address current problems in public health. This book is a series of essays that were collected to commemorate Richard and Joan Doll on the occasion of the former's retiring as Warden of Green College. It serves as a useful picture of current evidence relating to the epidemiology of cancer.

Most of the authors that contributed to the text are from Great Britain where they were teachers, colleagues, or students of Sir Richard. Epidemiology as a discipline developed in Great Britain, with the names of Graunt, Farr, and Snow preeminent in its history. The authors of this collection of essays continue the grand tradition of British epidemiology, which now addresses problems that are worldwide in scope. Thus, the subject of each of the chapters in this book is of great interest in determining the causes of cancer: smoking, diet, occupation, radiation, infections, hormones, and other drugs. Issues relating to the prevention of cancer are also addressed.

Forewords written by Sir Austin Bradford Hill and Sir Francis Avery Jones, a statistician and a clinician, respectively, describe how these leaders in medical investigation worked with Sir Richard in early studies of the epidemiology of lung cancer and peptic ulcers. A chapter written by Richard Peto is a summary of the landmark paper he coauthored with Doll in 1981 entitled, "The Causes of Cancer." The chapters by Paula Cook-Mozaffari on "The Geography of Cancer," Nicholas Wald on "Smoking," Bruce Armstrong and Jim Mann on "Diet," Rudolfo Saracci on "Occupation," Peter Smith on "Radiation," and Martin Vessey on "Exogenous hormones" refer to the important contributions that Sir Richard made in our understanding of these factors in the development of cancer. Each serves well as a springboard on which to base future research.

The ultimate aim of epidemiology is the prevention of disease, and chapters by Muir Gray and Charles Fletcher, by Gray and Konrad Jamrozik, and by Nigel Gray discuss how legislation and education will contribute to this effort. Again, the work of Sir Richard has provided important information toward these efforts.

While this book does not attempt to be as comprehensive as that edited by Schottenfeld and Fraumeni entitled, *Cancer Epidemiology and Prevention*, it is well suited as an introduction to cancer epidemiology. Thus, the interested clinician or medical student will find a concise and readable review of the important causes of cancer as viewed by the epidemiologists of today. As a tribute to Sir Richard Doll, the authors have succeeded in placing 40 years of his work in the context of today's knowledge.

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ONCOLOGIC IMAGING

Edited by David G. Bragg, MD, Philip Rubin, MD, and James F. Youker, MD. 664 pp, illustrated. Elmsford, NY, Pergamon Press, Inc, 1985. $125.00 (hardcover)

This large format book is, to the reviewer's knowledge, one of a kind, and would be an important addition to the reference libraries of both oncologists and those in radiology who spend a great deal of time caring for patients with cancer. The text is edited by three outstanding experts, and each chapter is written by an extremely qualified subspecialist. It is profusely illustrated, well organized, and extensively referenced.

For reasons that are not clear, the credentials of the editors and authors are not explicitly given. From personal knowledge, however, I know that each is an acknowledged expert in the areas on which they have written. The inclusion of numerous excellent magnetic resonance images is rather astonishing at this point in time.

A thorough coverage of all aspects of each tumor category is provided. This includes incidence, behavior, classification, staging, imaging procedures and assessments, and imaging strategies and decisions, as well as treatment. The impact of various technologic advances is discussed along with the possible impact of future oncologic advances and interventional radiography. Percutaneous biopsy has probably been the greatest advance in tumor management because it reduces the level of uncertainty of diagnosis to a minimum. The various techniques in each situation are explicitly outlined in this book.

It would have been helpful had the editors included common clinical problems such as isolated pleural effusions, how to evaluate them and, once malignancy is diagnosed, what further workup, if any, is indicated. Dealing with these problems, and so frequently at great cost, occupies a good part of the oncologist's daily life.

Admittedly, the authors indicate that controversy exists in the radiologic approach to cancer, and this is carefully exposed in a forthright manner. The section on staging of cancer is well covered, and appropriate modalities for staging and quantification are recommended. Decision trees are frequently displayed that assist in the evaluation of each clinical problem involving patients with cancer.

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CLINICAL RADIOLOGY OF THE SPINE AND SPINAL CORD

By Mohamed Banna, MD. 449 pp, illustrated. Rockville, Md, Aspen Systems Corp, 1985. $78.00 (hardcover)

The author's theme and purpose of this text is to share his neuroradiologic experiences in order to enhance the knowledge and skills of the readership. The author was until recently a professor of radiology at McMaster University Medical Center in Ontario, Canada and is now professor and chairman of radiology at King Faisel Specialist Hospital in Saudi Arabia. He trained at Atkinson Morley's Hospital in neuroradiology and has practiced neuroradiology during the intervening 20 years.

This book is a useful addition to the medical literature. It has a strong clinical orientation, utilizing short and concise explications of disease processes heavily annotated by images and line drawings. The book surveys developmental abnormalities and anomalies and traumatic, degenerative, vascular, and mass lesions. Infectious processes of the disc space and vertebrae are found in the chapter on the intervertebral disc.

Technical considerations of contrast material and imaging modalities including myelography, computed tomography, and magnetic resonance are presented. The topics are rationally organized, and the images are of uniformly good quality. The section on myelography and computed tomography highlights practical pertinent information and includes an excellent listing of phenothiazine derivatives. No mention is made of the newer less toxic, nonionic water soluble contrast materials: iopamidol and iohexol. Although these materials have been used in Europe for several years, they have only recently received approval from the FDA in the United States.

The section on injuries gives a brief but cogent description of the traumatic mechanisms producing the injury. Excellent line drawings simplify the descriptions of abnormalities. The chapter on the intervertebral disc is an excellent admixture of clinical and pathophysiologic highlights and radiographic findings. It also includes concise discourses on facet joints, ankylosing and other forms of spondylitis, and disc space and spinal infections. Intraspinal mass lesions are dealt with in a classical manner and are refreshingly annotated by clinical plain film changes that are often overlooked in this day of reliance on computed tomography and nuclear magnetic resonance.

The chapter on spinal dysraphism is replete with helpful line drawings and pathologic and operative material, and it presents pertinent, well-referenced theoretical possibilities to explain the abnormalities. Tumor and tumor-like conditions of the vertebral column are highlighted. The book is not meant to be an exhaustive treatise on the subject but is thoroughly referenced for further in-depth study.

There is a short chapter on magnetic resonance imaging co-authored by Armin Kuhnert. There is a brief overview of the physical principles and techniques followed by numerous images of a broad spectrum of pathologic entities.

This book is recommended as an excellent point of departure for the radiologist and those in the clinical neurosciences interested in the spine and its contents.

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STATE OF THE ART REVIEWS. OCCUPATIONAL MEDICINE. THE MICROELECTRONICS.

Edited by Joseph LaDou, MD. 197 pp, illustrated. Philadelphia, Hanley and Belfus, Inc, 1986. $22.00 (hardcover)

In the 40 years since their invention, microelectronic components have become commonplace. Both large and small companies have participated in this growth. As a result of the rapid growth and the proliferation of smaller companies, medical professionals must become familiar with the health care needs of workers in the microelectronics industry. The authors of this book elucidate clinical problems seen in these workers so that medical and research professionals can more adequately address the medical and scientific needs of this industry.

Providing occupational health care to workers in the microelectronic field requires an understanding of the semiconductor fabrication process. In discussing this process the authors expose two myths about the industry; that it is both clean and safe. Virtually every step of the fabrication process requires the use of exotic and toxic gases. High-use gases include nitrogen, argon, oxygen, and hydrogen with lesser quantities of numerous reactive gases such as arsine. The discussion of the use of these gases and engineering controls available convinces the reader that the microelectronics industry is not clean. Safety statistics, based on data from California, indicate that occupational illness accounts for 19.9% of all lost-work-time injuries and illness in the microelectronics industry as compared with 6.5% for the average of all manufacturing industries. Maintenance personnel, like their colleagues in manufacturing, are at greatest risk of exposure. The chapter that explains the details of the semiconductor fabrication process illustrates that health care issues are as significant for the microelectronics industry as for the manufacturing industry.

In any industry, the practice of occupational medicine involves both treating patients and ensuring that toxic exposures do not occur. The authors discuss six specific hazards of the microelectronics industry—gallium arsenide, photoactive chemicals, solvents, hydrofluoric acid, toxic gases, and radiofrequency and microwave radiation—and present medical findings and industrial hygiene data. In the clinical setting, workers present with specific complaints frequently focused on reproductive problems, cancer, and dermatitis. The authors discuss these issues with an emphasis on cause rather than on treatment.

This book is the first of the publisher's series entitled *State of the Art Reviews* in occupational medicine. Although 20 authors made contributions, the editor effectively integrated each topic into the text. Both clinicians and researchers will find this book a timely and informative review of the health issues facing workers in the microelectronics industry. With the growing importance of this industry in the marketplace, all health care providers should be aware of the concepts presented in this book. These workers will increasingly constitute an important segment of the nation's workforce.

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COMPUTER APPLICATIONS IN CLINICAL PRACTICE. AN OVERVIEW

Edited by Daniel Levinson, MD. 331 pp, illustrated. New York, Macm' ı Publishing Co, 1985. $29.95 (paperback)

Rapid advances in computer technology have led to widespread availability of powerful micro or "desk-top" computers at increasingly lower costs. This in turn is leading to the rapid expansion of computer applications in clinical medicine. Applications that could only have been possible on large and prohibitively expensive computers a decade ago can be routinely carried out on today's microcomputers. Physicians are faced with an ever-expanding body of medical knowledge that makes the practice of medicine an increasingly complex task. This is further complicated by the great amount of administrative activity necessary to provide quality health care. The modern microcomputer can and will become an in-

creasingly valuable aid to the practicing physician in both of these areas.

Physicians in the past have been reluctant to accept the computer as an aid in clinical practice. This attitude may be largely due to a general lack of computer literacy among many physicians. This book is primarily written for this audience and provides a clear and readable overview of the microcomputer and its various applications in clinical medicine. The book focuses on two major areas: computer structure and function, and applications in specific areas of clinical practice.

The chapters on computer structure and function provide the reader with an understanding of how the computer works as well as an understanding of the various ancillary components that comprise a modern microcomputer system. The authors provide the reader with a comprehensive overview of the microcomputer and demystify most of the computer jargon that can prove so frustrating to the uninitiated. The reader is also provided with a wealth of practical information on the selection of proper hardware and software when purchasing a microcomputer.

The second major focus of the book is an introduction to the various uses or applications of the computer in clinical practice. Applications that are currently in use and those that remain experimental are presented for most medical specialties. Although applications for some specialties are presented in a somewhat sketchy manner, the book provides the reader with a basic framework. Numerous references and other resources for information regarding specific applications are provided and will be useful to the reader who wishes to pursue a specific application in more depth. Applications in pharmacy, nursing, patient care, clinical information management, and medical education are also covered.

Other topics presented include ergometric and psychosocial considerations, a listing of current on-line medical literature data base services and how to access them, and an extensive bibliography that provides a useful source of further information for the topics covered in the book.

Dr Levinson has succeeded in compiling a book that will give readers a sound foundation in understanding and using microcomputers as well as an introduction to various computer applications in clinical medicine. The book is well written and extremely readable and should provide valuable information to the physician with little or no knowledge of computers.

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WE ARE NOT ALONE: LEARNING TO LIVE WITH CHRONIC ILLNESS

By Sefra Kobrin Pitzele. 306 pp, illustrated. Minneapolis, Minn, Thompson and Co, 1985. $14.95 (paperback)

Written from the perspective of her own personal battle with systemic lupus erythematosis, Sefra Kobrin Pitzele compassionately offers guidance on how to live with a chronic illness. Deftly mixing practical advice with emotionally uplifting poetry and quotes, the author touches all of the bases leading to the readjustment process for the patient, the family, and the rest of the world. Humorous cartoons also lighten the serious nature of the book while still making relevant points. Furthermore, there are quick and easy meal recipes; transportation listings for automobile and other forms of travel; listings of helpful organizations, products, and services, including toll-free numbers; a sample of a bill of rights for patients; a consultant and technical term glossary; a bibliography of popular books, pamphlets, and medical journal articles; and an index for locating special interests.

An unusual feature of this book is a reader survey meant to be detached and returned. Ms Pitzele states that she intends to write more about chronic illness and asks readers to supply data about their medical conditions, family, dissatisfactions, relationships, work, living situation, insurance, support groups, as well as opinions about the book and the author.

Early in the book, the author notes that life is not always fair in deciding who gets sick and who remains healthy. Then, establishing the fact that the book is about everyone and not merely the author, she proceeds to discuss the diagnosis, the grieving process, and the explanation of the chronic illness to family and friends. Stress, illness, and pain as cycles of events are intermingled with details about the health care team, the caregivers, and the normal feelings of depression. From here, the book moves into adjustments in living and discusses methods for relaxation, sexual concerns, exercise, and insurance. Of particular concern is a chapter on adaptive living strategies. Specific modifications are described and illustrated for the kitchen, the bedroom, the bathroom, the laundry room, yard work, and the automobile.

This book is striking for its insights into coping with chronic illness as well as for the inspirational tone that uplifts the downtrodden human spirit. The author graphically illustrates that individuals can move mountains if they believe in themselves. True, the support system, the love, the friendship, and the medical care all play a part. But first the individual has to come to terms with his or her own condition.

In addition, this book is produced in a highly readable style with large print and plenty of white space. There are also numerous short anecdotes that illustrate salient points.

All told, this comprehensive, reasonably priced paperback should be most appealing for physicians to recommend to chronically ill patients and their families. There is no doubt that the book will supply patients with the practical information as well as the inspiration needed to cope with their illness. More importantly, the book can provide the appropriate regimen for readjustment. This book may literally demonstrate that the pen is mightier than the sword, or in this case, mightier than the pill and the machine.

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Jones' commission on liability insurance makes report to governor

Governor Mario M. Cuomo's special advisory commission on liability insurance filed its report in early April 1986, surprising the governor and encouraging concerned parties by recommending a $250,000 cap on noneconomic damages in suits against municipalities and other nonprofit groups. Although the recommendation for the cap did not include suits against physicians, it was viewed by the medical community as a positive step toward viable liability reform. Governor Cuomo and the Democrat-controlled assembly have rejected the cap as part of any liability reform legislation in the past, while the Republican-controlled senate has supported it.

"There are two largely independent forces at work: an industry business cycle that creates incentives for sudden and, too often, intolerable price swings, and rapidly rising liability costs, which will push the price trend sharply upward over time. Any meaningful and lasting solution must address both sides of the coin," said Judge Hugh R. Jones, chairman of the commission, in a press release.

The recommendations in the commission's report focused on two areas: tighter regulation and control of the insurance industry and significant changes in tort law and procedures. Although the recommendations of the commission were intended to address problems of municipal liability, some are applicable to other areas of liability as well. The tort reform recommendations of the commission include the following:

- amendment of joint and several liability doctrine;
- abolition of the collateral source rule;
- ceiling on recovery for certain noneconomic damages (pain and suffering) from public entities;
- protection of directors and officers of not-for-profit corporations;
- frivolous suit sanctions;
- structured awards; and
- separating the issue of liability from the nature and extent of damages in trials, thereby minimizing the need for unnecessary trials and maximizing settlement incentives.

Governor Cuomo praised the work of the commission and endorsed many of its recommendations, but retained his previous position on the proposal to cap noneconomic damage awards. In a statement released following the announcement of the commission's findings, Cuomo said, "... the commission has not made a persuasive case in support of a proposed cap of $250,000 on noneconomic awards. There is no demonstration that the cap is necessary ... I recommend we not consider such a step, unless there is a clear showing that no other alternative is available and the insurance industry finds a way to guarantee that this drastic limitation on our system of justice would produce savings that establish a cost-benefit justification."

Although the governor seemed to reject the recommendation for the cap, John A. Finkbeiner, president of the Medical Society of the State of New York, found a grain of hope in the governor's "qualified rejection."

"We believe the case [for the cap] can and, in fact, already has been made and we hope that it will be brought to the Governor's attention by the commission and others in such a way that the justification for the cap will be so clearly drawn that he too will be convinced," Finkbeiner said. "The Commission was right in adopting the concept of limiting pain and suffering awards, but that concept should be applied to all forms of liability including medical liability. No segment of the economy can continue to support a sky-is-the-limit approach in these cases."

Cuomo proposes stiffer regulation for physicians

Less than a week after 2,000 physicians gathered in Albany to press Governor Mario M. Cuomo for meaningful remedies to the malpractice crisis, Cuomo responded—but not in the manner physicians had hoped for.

Cuomo's response was to the malpractice caused by incompetent physicians who go unchecked by state regulatory agencies. He proposed that physicians should have to pass periodic competency reviews in order to retain their licenses to practice in New York. "Many citizens are disturbed by reports of misconduct among doctors. This reform effort will put in place the strongest system of quality control anywhere in the country," Cuomo said in a news conference at his World Trade Center office, where he announced the proposals on May 28th. He was joined at the conference by Dr David Axelrod, commissioner of health; John Cardinal O'Connor, the archbishop of New York; Andrew J. Stein, city council president; and Rudolph W. Giuliani, the United States attorney in Manhattan. "Our objective is to reduce the number of injuries and deaths suffered by New Yorkers as a result of negligence or incompetence by the medical profession," Stein said at the conference.

If the proposal were implemented, New York would be the first state to make reviews mandatory for license renewal. Cuomo's proposal has the support of Martin Burrell, chancellor of the board of regents; Burrell said he would recommend approval to the board. The board of regents alone would need to approve the proposals; implementation of the proposals would require legislative action.

The following measures were also proposed by Cuomo:

- requiring medical malpractice companies to report physicians who have a large number of successful claims against them, and requiring hospitals to report any cases of medical misconduct against physicians
- suspending the license of any physician convicted of assault or other crimes against a patient
- giving patients the right to obtain and review their medical records
- intensifying the State Health Department's hospital inspection programs by assigning inspectors to interview patients about the care they receive. These reports would supplement the reports of the Joint Commission for the Accreditation of Hospitals, the Chicago-based organization that reviews most hospi-

NEWS BRIEFS are compiled and written by Sandra Cirincione.

tals in the country. (This proposal would not require legislative action.)

Responses to the governor's proposals from the medical community thus far have been reserved, as officials await more details. Otis R. Bowen, MD, secretary of the Department of Health and Human Services, said he thought Cuomo's proposals went "a little too far." Dr Bowen said existing procedures, such as continuing medical education and reviews by medical specialty boards, were already in place to assure physician competency.

John A. Finkbeiner, MD, president of the Medical Society of the State of New York, said that some of Cuomo's proposals duplicated already existing procedures. "Hospital privileges, a virtual requirement for the practice of medicine, are granted only to those physicians who have demonstrated their competency to medical staff department chiefs and to quality assurance committees. . .and may be revoked at any time," Dr Finkbeiner said in a statement on the proposals.

New York Public Health law mandates hospital involvement in the credentialling of physicians and in quality assurance, and already requires hospitals to report any termination, suspension, or restriction of hospital privileges, or any information that reasonably shows a physician is guilty of misconduct, Dr Finkbeiner said. Similarly, medical liability insurance companies are required to report every malpractice claim filed against a physician, and to report again if the judgment is decided in favor of the plaintiff, he said. While welcoming the interest of the governor on the issue of quality of care assurance, Dr Finkbeiner admonished, "It is imperative that a distinction be made between misconduct and malpractice. It has been clearly established that our most competent physicians and hospitals are frequently sued for malpractice, not because they are negligent or incompetent but because they perform high-risk procedures."

While New York officials plan for new regulations, the federal government is also studying ways to improve its system for finding and disciplining incompetent physicians. Richard J. Kusserow, inspector general of the Department of Health and Human Services, reported to Dr Bowen that state medical licensing boards, which oversee the licensing of physicians, were too understaffed to deal with increasing physician discipline and incompetency caseloads. Kusserow's report suggested that physician license renewal fees be increased, with the additional funds being used to increase the staffs of professional medical boards. The report also included the following recommendations:

- giving federal peer review groups that monitor federally financed health care the legal authority to report to state medical boards cases involving physician misconduct or incompetency
- urging hospitals to be more active in reporting such cases to state health authorities
- giving the Department of Health and Human Services the power to exclude from Medicare, the federal health program for the elderly, and Medicaid, the program for the poor, any physician whose license has been revoked or suspended
- limiting federal medical education aid to students in US or Canadian medical schools
- creating a centralized national accrediting procedure for foreign medical schools
- establishing a licensing procedure for interns in hospital training programs

The release of the report coincided with Dr Bowen's address to the graduating class of New York University's School of Medicine, in which he encouraged the new physicians to report the poor practice of medicine if they saw it. "Nowhere near enough" physicians were being disciplined for incompetence, he told the graduates, and organized medicine "can no longer abide a brotherhood of silence" on the issue, he said.

James H. Sammons, MD, executive vice president of the American Medical Association (AMA), disagreed with Bowen that a large number of physicians were escaping disciplinary action, or that there was any "conspiracy of silence" among physicians. However, he praised the report of the inspector general and said the AMA would support its recommendations.

Supreme Court strikes down "Baby Doe" rules

The United States Supreme Court dealt a blow to the Reagan administration by invalidating the "Baby Doe" rules, which required hospitals to provide life-prolonging care to severely handicapped newborn infants.

In a plurality decision joined by three other justices, Associate Justice John Paul Stevens asserted that there was no evidence of discrimination by hospitals in the provision of care to handicapped infants, and thus the federal government's intervention in the issue was inappropriate.

The so-called "Baby Doe" rules arose from the 1983 case of a Long Island couple who decided after consultation with physicians not to seek corrective surgery for their infant daughter, who was born with spina bifida and other birth defects. The Department of Health and Human Services sought access to hospital records to insure that the infant, who became known in the courts as "Baby Jane Doe," was not being refused care because she was handicapped. A 1973 federal statute prohibits discrimination against handicapped persons by organizations that receive federal funds.

The "Baby Doe" rules required hospitals to provide government investigators expedited access to hospital records and facilities to insure that handicapped infants were not discriminated against in decisions regarding life-prolonging care. The rules also required hospitals to post notices encouraging staff members to report any suspected instances of discrimination against handicapped infants in care decisions.

Two federal courts had previously ruled against the regulations, and the Reagan administration did not appeal the case. The American Hospital Association, the American Medical Association, and other medical groups pursued the case to the nation's highest court.

The Court's approach to the decision was from a strictly legal point of view, examining only the appropriateness of the application of the federal statute. In writing his decision, Justice Stevens did not deal with the moral questions of what rights handicapped infants possess, under what

circumstances a handicapped infant should be denied life-prolonging treatment or nourishment, or who should make such a decision.

Justice Stevens rejected the federal regulations on the grounds discrimination had not occurred against any infants because no hospital had refused treatment that had been sought by parents. The federal regulations were ruled intrusive because they superseded state regulations and child neglect laws that were already in place to protect infants in cases of abuse or neglect, Justice Stevens said.

Justice Stevens said the 1973 law did not require federal regulators "to give unsolicited advice either to parents, to hospitals or to state offices who are faced with difficult treatment decisions concerning handicapped children." The federal government will no longer be able to mandate the treatment of an infant against the wishes of the parents or best judgment of the physicians.

Justices Harry Blackmun, Thurgood Marshall, and Lewis Powell concurred with the opinion written by Stevens. Chief Justice Warren Burger cast the fifth vote in favor of the decision, but did not join in Steven's opinion or give any reason of his own for his decision. The dissenting justices were William Brennan, Sandra Day O'Connor, and Byron White.

MEDICAL SOCIETY NEWS

Policy adopted on withholding and terminating life sustaining apparatus

The Council of the Medical Society of the State of New York recently adopted the following statement regarding the withholding and terminating of life-sustaining apparatus:

> In the care of the terminally ill and in the service of human dignity the physician's ethical role includes the provision of comforts as well as healing. Traditionally, hydration by mouth or vein and oral or tube feeding have been considered to be part of overall supportive care not different from skin care, bowel and bladder care, grooming and psycho-social support. It thus follows that the withholding or withdrawal of fluids and nutrition from a terminally ill patient is ethically wrong.
>
> An alternate view is that tube feeding and intravenous hydration are medical treatments not different from antibiotics, respirators, oxygen or hemodialysis. According to this view, when medical treatment is no longer considered appropriate, it is morally justified to withdraw or withhold intravenous fluids and tube feeding.
>
> Since this issue is complex and difficult and entails not only medical and legal aspects, but moral and religious sensitivities, it seems prudent that each case be evaluated, discussed, and decisions made on the individual merits of each case. It is suggested that, where necessary and appropriate, hospital medical ethics committees be consulted for guidance and advice.

Changes in Executive Committee meeting policy

The Council of the Medical Society of the State of New York recently voted to approve the suggestion of Society President John A. Finkbeiner, MD, that the executive committee, consistent with the bylaws, henceforth shall meet only in case of emergency arising in the interim between meetings of the council. In the past, the executive committee met prior to each council meeting. In accordance with Dr. Finkbeiner's suggestion, two executive committee meetings were scheduled for the months of July and August, during which the council does not meet. When council meetings resume in September, meetings of the executive committee will be subject to the above recommendation.

MEDICAL SOCIETY NEWS is written by Sandra Cirincione.

OBITUARIES

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Jacob Harold Ackerman, MD, White Plains. Died January 26, 1986; age 82. Dr Ackerman was a 1929 graduate of the University of Maryland School of Medicine, Baltimore. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Nathan Bercovitz, MD, Miami Beach, Florida. Died April 19, 1986; age 84. Dr Bercovitz was a 1932 graduate of the University of Maryland School of Medicine, Baltimore. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Eugene Y. Berger, MD, Bronx. Died March 23, 1986; age 67. He was a 1944 graduate of the New York University College of Medicine. Dr Berger was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the Academy of Medicine, the American Society for Clinical Investigation, the Bronx County Medical Society, and the Medical Society of the State of New York.

Charles Buckman, MD, Flushing. Died April 4, 1986; age 86. Dr Buckman was a 1922 graduate of McGill University Faculty of Medicine, Montreal. He was a Fellow of the American Psychiatric Association, a Diplomate of the American Board of Psychiatry and Neurology, and a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Ralph A. Camardella, MD, Malverne. Died April 13, 1986; age 75. He was a 1938 graduate of Georgetown University School of Medicine. Dr Camardella was a Fellow of the American Academy of Family Practice and a member of the Academy of Medicine, the New York Cardiological Society, the American Occupational Medical Association, the Nassau County Medical Society, and the Medical Society of the State of New York.

George S. Cattanach, MD, New York. Died March 28, 1986; age 88. He was a 1924 graduate of Johns Hopkins University School of Medicine, Baltimore. Dr Cattanach was a member of the American Psychiatric Association, the American Geriatrics Society, the Association for Research in Nervous and Mental Disease, the New York County Medical Society, and the Medical Society of the State of New York.

Avedis Cetin, MD, Woodbury. Died March 6, 1986; age 57. Dr Cetin was a 1955 graduate of the University of Istanbul Medical Faculty-Istanbul Universitesi Tip Fakultesi. Dr Cetin was a Fellow of the American College of Anesthesiologists and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Nassau County Medical Society, and the Medical Society of the State of New York.

Robert L. Clarke, MD, New York. Died April 15, 1986; age 60. He was a 1950 graduate of Cornell University Medical College. Dr Clarke was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Surgery. His memberships included the New York State Surgical Society, the Academy of Medicine, the American Association for the Surgery of Trauma, the New York County Medical Society, and the Medical Society of the State of New York.

William Vito Colangelo, MD, Aiken, South Carolina. Died March 21, 1986; age 82. Dr Colangelo was a 1938 graduate of Middlesex University School of Medicine, Waltham. He was a Fellow of the American College of Emergency Physicians and a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Socrates Constantinou, MD, White Plains. Died April 22, 1986; age 51. He was a 1965 graduate of the National and Capodestrian University Faculty of Medicine, Athens. Dr Constantinou was a Fellow of the American Psychiatric Association and a member of the American Society of Adolescent Psychiatry, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

William Ebner, MD, Bronx. Died January 29, 1986; age 88. Dr Ebner was a 1922 graduate of Eotvos Lorand Tudomanyegyetem Orvostudomanyi Fakultas, Budapest. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Joseph William Finn, MD, Brooklyn. Died April 21, 1986; age 75. He was a 1938 graduate of the State University of New York Downstate Medical Center, Brooklyn. Dr Finn was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Medical Society of the County of Kings and the Medical Society of the State of New York.

Irwin F. Forbes, MD, Surfside, Florida. Died March 29, 1986; age 81. Dr Forbes was a 1929 graduate of Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin. He was a member of the American Academy of Family Practice, the American Geriatrics Society, the Medical Society of the County of Herkimer, and the Medical Society of the State of New York.

Margot L. Forbes, MD, Surfside, Florida. Died March 29, 1986; age 80. She was a 1930 graduate of Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin. Dr Forbes was a member of the American Academy of Family Practice, the American Geriatrics Society, the Medical Society of the County of Herkimer, and the Medical Society of the State of New York.

Madeline Fries, MD, Massapequa. Died April 15, 1986; age 90. Dr Fries was a

1921 graduate of Cornell University Medical College. She was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Hans W. Goldschmidt, MD, Hillside, New Jersey. Died March 30, 1986; age 88. Dr Goldschmidt was a 1924 graduate of Schlesische-Friedrich-Wilhelms Universitat Medizinische Fakultat, Breslau. He was a member of the American Academy of Family Practice, the Nassau County Medical Society, and the Medical Society of the State of New York.

Ahmad Haddad, MD, Sunnyside. Died April 5, 1986; age 76. Dr Haddad was a 1936 graduate of Madresseh Teb-Government Medical School, Teheran. Dr Haddad was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Frank Charles Hoak, MD, Kenmore. Died March 25, 1986; age 76. He was a 1936 graduate of the University of Buffalo School of Medicine. Dr Hoak was a Diplomate of the American Board of Dermatology, Inc, and a member of the Academy of Medicine, the New York State Dermatological Society, the American Academy of Dermatology, the Society for Investigative Dermatology, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Thomas Charlton Hobbie, MD, Sodus. Died March 11, 1986; age 82. Dr Hobbie was a 1933 graduate of the University of Buffalo School of Medicine. He was a member of the American School Health Association, the Medical Society of the County of Wayne, and the Medical Society of the State of New York.

Francis D. Kane, MD, New York. Died March 10, 1986; age 71. He was a 1940 graduate of the University of Buffalo School of Medicine. Dr Kane was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

James Patrick Kinney, MD, Tonawanda. Died April 5, 1986; age 93. Dr Kinney was a 1920 graduate of the University of Maryland School of Medicine, Baltimore. His memberships included the Medical Society of the County of Erie and the Medical Society of the State of New York.

John Gaspare Lipani, MD, Brooklyn. Died January 20, 1986; age 79. He was a 1929 graduate of Tulane University School of Medicine, New Orleans. Dr Lipani was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Ophthalmology, and a member of the American Academy of Ophthalmology and Otolaryngology, the Pan American Medical Association, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Louis Mamelok, MD, New York. Died March 30, 1986; age 95. Dr Mamelok was a 1916 graduate of Columbia University College of Physicians and Surgeons. He was a member of the American Academy of Allergy, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

James Pratt Marr, MD, New York. Died April 23, 1986; age 88. He was a 1924 graduate of the University of Vermont College of Medicine, Burlington. Dr Marr was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Academy of Medicine, the New York Obstetrical Society, the New York County Medical Society, and the Medical Society of the State of New York.

John H. McClement, MD, New York. Died April 8, 1986; age 68. Dr McClement was a 1943 graduate of the University of Rochester School of Medicine and Dentistry. He was a Fellow of the American College of Physicians, a Diplomate of the American Board of Internal Medicine, and a member of the American Thoracic Society, the New York County Medical Society, and the Medical Society of the State of New York.

Nathan Moros, MD, Long Island City. Died January 28, 1986; age 79. He was a 1933 graduate of New York University College of Medicine. Dr Moros was a member of the American Psychiatric Association, the American Academy of Family Practice, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Vincent James Palmeri, MD, Newark. Died March 2, 1986; age 77. Dr Palmeri was a 1935 graduate of the St Louis University School of Medicine. He was a Fellow of the American Academy of Family Practice, a Diplomate of the American Board of Family Practice, and a member of the American Geriatrics Society, the Medical Society of the County of Wayne, and the Medical Society of the State of New York.

Albert Dorian Parets, MD, New York. Died April 4, 1986; age 76. He was a 1936 graduate of New York University College of Medicine. Dr Parets was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the New York State Society of Internal Medicine, the Pan American Medical Association, the American Geriatrics Society, the New York County Medical Society, and the Medical Society of the State of New York.

George L. Rutherford, MD, Endwell. Died March 24, 1986; age 68. Dr Rutherford was a 1945 graduate of Georgetown University School of Medicine. He was a member of the Academy of Medicine, the American Academy of Occupational Medicine, the Broome County Medical Society, and the Medical Society of the State of New York.

Saul Schapiro, MD, New Rochelle. Died December 30, 1985; age 88. He was a 1923 graduate of Yale University School of Medicine. Dr Schapiro was a member of the New York Gastroenterological Society, the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Max Michael Simon, MD, Pleasant Valley. Died April 5, 1986; age 87. Dr Simon was a 1925 graduate of Cornell University Medical College. He was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a member of the Dutchess County Medical Society and the Medical Society of the State of New York.

Francis Sisca, MD, New York. Died March 29, 1986; age 84. Dr Sisca was a 1929 graduate of New York Medical College, Flower and Fifth Avenue Hos-

pitals. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Stuart Alan Stein, MD, Bayside. Died April 17, 1986; age 44. He was a 1973 graduate of Escuela de Medicina Univers Nacional Pedro Henriquez Urena, Santo Domingo. Dr Stein was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Eugene F. Vitagliano, MD, Brooklyn. Died January 31, 1986; age 85. He was a 1927 graduate of the State University of Iowa College of Medicine, Iowa City. Dr Vitagliano was a Fellow of the American College of Surgeons and a member of the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Paul P. Welsh, MD, LeRoy. Died April 12, 1986; age 79. Dr Welsh was a 1933 graduate of Georgetown University School of Medicine. He was a Diplomate of the American Board of Internal Medicine and a member of the Medical Society of the County of Genesee and the Medical Society of the State of New York.

Evan H. Wright, MD, Brooklyn. Died August 19, 1985; age 60. He was a 1960 graduate of the Universite de Paris Faculte de Medecine. Dr Wright was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Medical Society of the County of Kings and the Medical Society of the State of New York.

IN MEMORIAM

Frances Casey, who served on the *Journal* in the area of editorial production for 30 years—from 1952 to 1982—died on March 6, 1986. A memorial service was held on March 22, 1986 at All Saints Church in New York City.

Elizabeth (Libby) Smith, who served as Managing Editor of the *Journal* from March 1968 until December 1980, died in early May 1986. She had previously served on the *Journal* staff in various capacities for several years. A memorial service was held on June 4, 1986 at the Madison Avenue Presbyterian Church in New York City.

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The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089–1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

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A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

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Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

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The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

References

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

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The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear on the text. When there are six or fewer authors, all should be listed; where there are seven or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83:925–927.
2. McGuigan JE. Peptic ulcer. In: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD, eds. *Harrison's Principles of Internal Medicine*. New York, McGraw-Hill, 1983, pp 1697–1712.

Review

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

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Sept 25–26. **Advances in Treatment of Leukemia and Marrow Stem Cell Disorders.** 9 Cat 1 credits. Sheraton/Wharf Hotel, San Francisco. Info: University of California, Room 575-U, San Francisco, CA 94143-0766. Tel: (415) 476-5808.

Sept 25–27. **Myocardial Dysfunction in Ischemic Heart Disease: Medical and Surgical Considerations.** 17 Cat 1 credits. Hotel Inter-Continental, San Diego. Info: Office of Continuing Medical Education, M-017, UC San Diego School of Medicine, La Jolla, CA 92093. Tel: (619) 534-3940.

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Sept 7–13. **Doppler and 2-D Echocardiology.** 40 Cat 1 Credits. Info: James L. Weiss, MD, The Johns Hopkins University School of Medicine, Baltimore, MD 21205. Tel: (301) 955-5993.

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Sept 17–19. **American Cancer Society—National Conference on Gynecologic Cancer—1986.** 16½ Cat 1 Credits. Info: American Cancer Society—National Conference on Gynecologic Cancer—1986, 90 Park Ave, New York, NY 10016. Tel: (212) 599-8200.

KENTUCKY

Sept 12–14. **Multispecialty Oculoplastic Surgery Symposium.** 12 CME credits. Lexington Marriott Resort Hotel, Lexington. Info: Dr Constance M. Fulmer, Good Samaritan Hospital, Lexington, KY 40508. Tel: (606) 252-6612, ext 3156.

MASSACHUSETTS

Sept 3–5. **Risk Analysis in Environmental Health—with Emphasis on Carcinogenesis.** Info: Harvard University, School of Public Health, Department A, 677 Huntington Ave, Boston, MA 02115. Tel: (617) 732-1171.

MICHIGAN

Sept 11–13. **International Symposium on Implant Arthroplasty for the Hand, Upper Extremity, and Foot.** 18 Cat 1 credits. Amway Grand Plaza Hotel, Grand Rapids. Info: G. Swanson, MD, 1900 Wealthy, SE, Suite 290, Grand Rapids, MI 49506. Tel: (616) 774-0191.

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TEXAS

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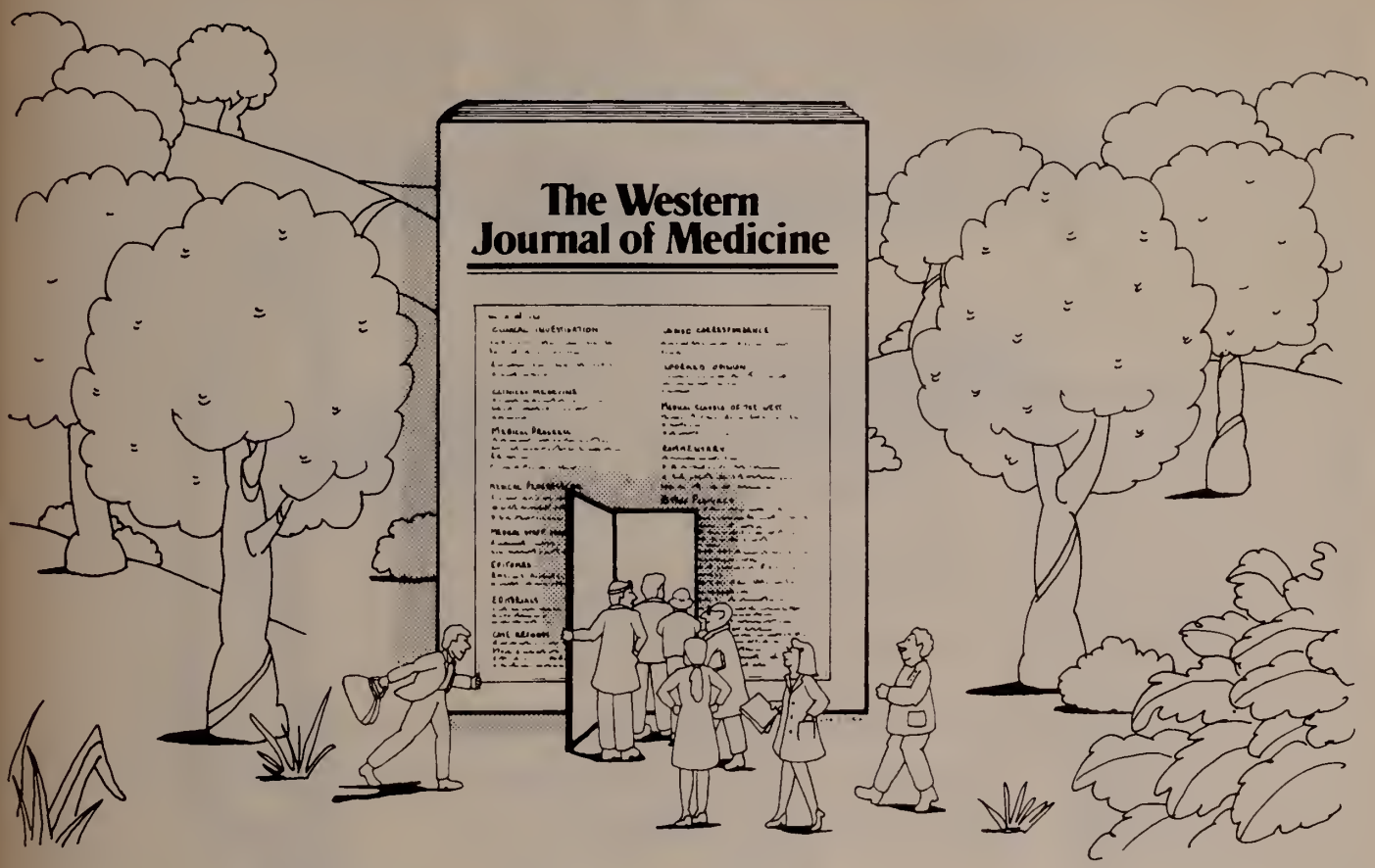

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CIGARETTE SMOKING, TOBACCO, AND HEALTH

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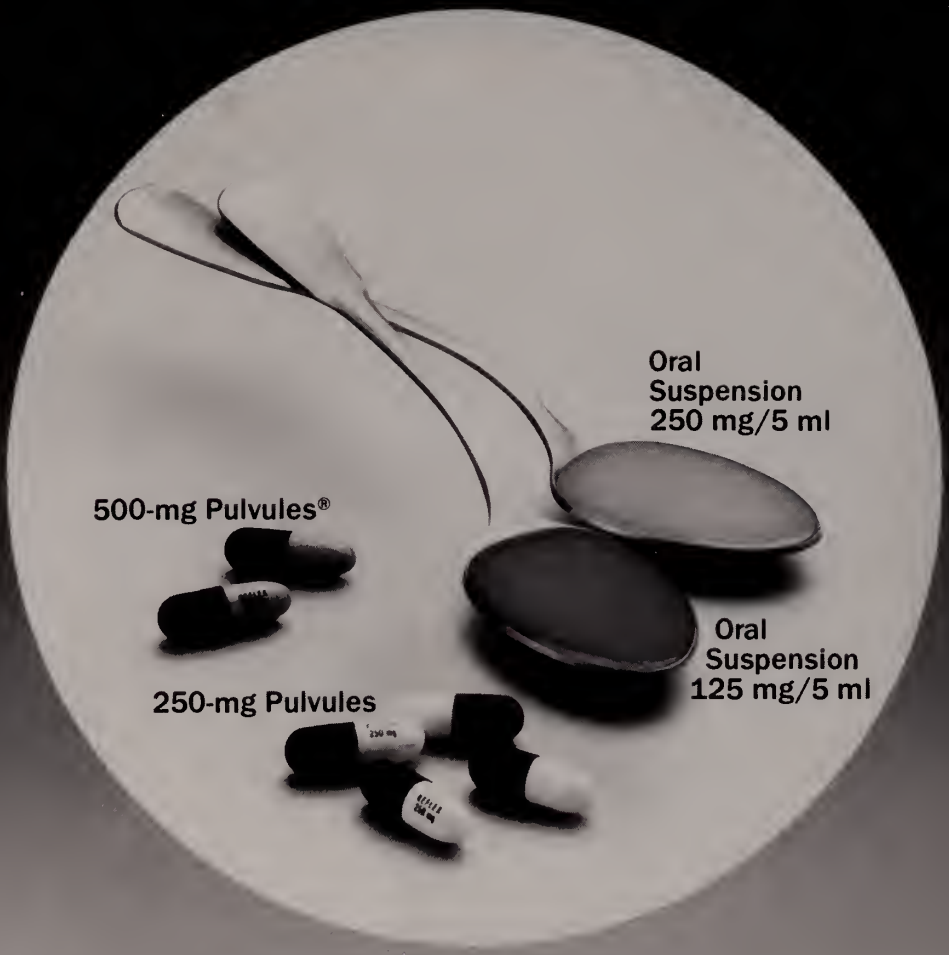

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Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)
Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.
Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.
Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration at doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.
There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.
Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.
Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.
In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.
The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. Issued 11/85
See complete Professional Use Information before prescribing.

References: 1. Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983; 106(6):1341-1347. **2.** Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984;24(Dec):150-159. **3.** Johnston DL, Lesaway R, Humen DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985;55:680-687. **4.** Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. **5.** Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982;50(Sept):94-116.

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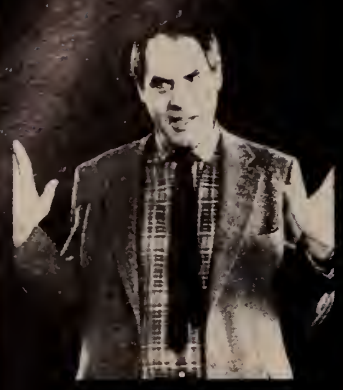

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OCTOBER 1986

AROUND THE STATE

MANHATTAN

Oct 9–10. **9th Annual Current Concerns in Adolescent Medicine.** 12 Cat 1 Credits. The Warwick Hotel. Info: Ann J. Boehme, Associate Director for Continuing Education, Schneider Children's Hospital of Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Oct 9–11. **18th Annual Oculoplastic and Facial Surgery Dissection Course.** Info: Congress Administrator, c/o Pierre Guibor, MD, 630 Park Ave, New York, NY 10021. Tel: (800) 223-4500.

Oct 10–11. **Functional Endoscopic Sinus Surgery.** 14 Cat 1 Credits. Info: Kristen Johnson, Administrator, Department of Otolaryngology, Manhattan Eye, Ear and Throat Hospital, 210 E 64th St, New York, NY 10021. Tel: (212) 838-9200, Ext 2448.

Oct 16–17. **Modulation of Immune System in Disease States and Organ Transplantation.** 12 Cat 1 Credits. New York Marriott Marquis. Info: Amir Tejani, MD, Box 49, SUNY Health Science Center at Brooklyn, 450 Clarkson Ave, Brooklyn, NY 11203. Tel: (718) 270-1090.

Oct 17. **Cosmetology Symposium.** *Oct. 28.* **Current Controversial Problems in Endocrinology.** Info: Beverley R. Baptiste, Medical Education, Beth Israel Medical Center, First Avenue at 16th St, New York, NY 10003. Tel: (212) 420-2849.

Oct 17–18. **Current Diagnostic and Therapeutic Management of Gynecologic Cancer.** 10 Cat 1 Credits. *Oct. 18.* **Echocardiography for the Internist.** 5¾ Cat 1 Credits. *Oct. 27–29.* **Sonography.** 17½ Cat 1 Credits. *Oct. 30–31.* **Interventional Radiology.** 13¼ Cat 1 Credits. NYU Medical Center—Alumni Hall Auditorium. Info: Registration Office, NYU Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Oct 23–25. **Intensive Care Medicine 1986—Attention to the Critical Details.** 20 CME Cat 1 Credits. Loews Summit Hotel. Info: Michael S. Niederman, MD, Course Director, Winthrop-University Hospital, Pulmonary and Critical Care Medicine Division, 259 First St, Mineola, NY 11501. Tel: (516) 663-2004.

NASSAU

Oct 15. **A Clinical Day in Ophthalmology: Corneal Diseases and Keratorefractive Surgery.** 7 Cat 1 Credits. The Garden City Hotel, Garden City. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

QUEENS

Oct 22–24. **The Surgical Treatment of Anorectal Malformations.** 21 Cat 1 Credits. Schneider Children's Hospital of Long Island Jewish Medical Center. Info: Ann J. Boehme, Associate Director for Continuing Education, Schneider Children's Hospital of Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Oct 30–31. **The Age of Geriatric Rehabilitation Perspectives and Potentials.** 15 Cat 1 Credits. Auditorium—Jewish Institute for Geriatric Care. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

ALBANY

Oct 23–24. **The Saphenous Vein Used In-Situ as an Artificial Bypass.** 10 Cat 1 Credits. Albany. *Oct 30.* **30th Anniversary Symposium ECOG and Cancer Control.** 7 Cat 1 Credits. Albany. *Oct 31.* **Respiratory Disease.** 7 Cat 1 Credits. Saratoga Springs. Info: Maureen A. Darragh, Acting Director, Office of Continuing Medical Education, Albany Medical College, 47 New Scotland Ave, Albany, NY 12208. Tel: (518) 445-5828.

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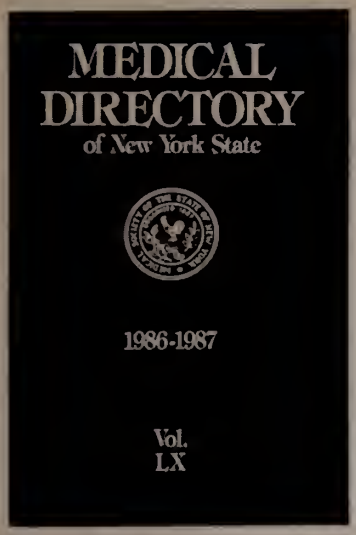

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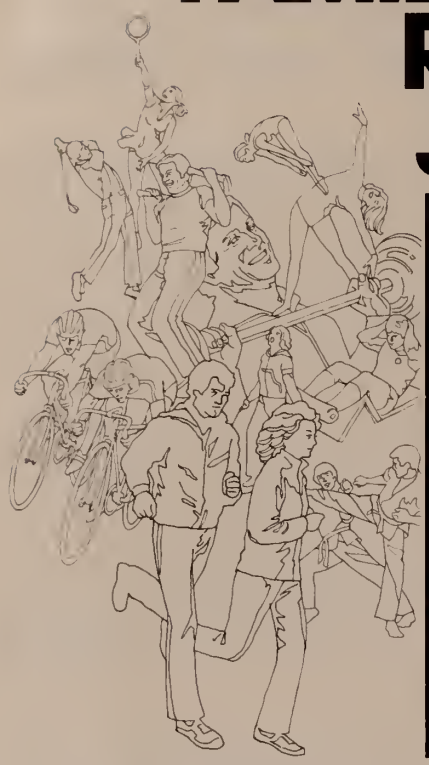

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Oct 3. **Trends in Management of Advanced Prostate Cancer.** Qualifies for Cat 1 Credits. Info: Gayle Bersani, RN, Coordinator of Continuing Education Programs, Education Department, Roswell Park Memorial Institute, 666 Elm St, Buffalo, NY 14263. Tel: (716) 845-2339.

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CALIFORNIA

Oct 6–10. **The 11th Annual San Diego Postgraduate Radiology Course.** 24 Cat 1 Credits. Hotel Del Coronado, Coronado. Info: Dawne Ryals, Ryals & Associates, PO Box 920113, Norcross, GA 30092-0113. Tel: (404) 641-9773.

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Oct 11–12. **The Skin from A to Z.** 10 Cat 1 Credits. Conference Center, UCSF Laurel Heights Campus. *Oct 16–18.* **Practical Topics in Pediatric Nutrition.** 13 Cat 1 Credits. Crystal Ballroom, The San Franciscan Hotel. Info: Registration Office, Room 575-U, University of California, CA 94143-0764. Tel: (415) 476-4251.

Oct 17–19. **Current Advances in Pediatrics.** Disneyland Hotel, Anaheim. Info: OCPS/California Chapter 4, AAP, PO Box 1297, Orange, CA 92668. Tel: (714) 978-2415.

Oct 30–Nov 1. **Imaging Symposium.** 14 Cat 1 Credits. US Grant Hotel, San Diego. Info: Dawne Ryals, Ryals and Associates, PO Box 920113, Norcross, GA 30092-0113. Tel: (414) 641-9773.

DISTRICT OF COLUMBIA

Oct 30–Nov 1. **Noninvasive Vascular Diagnostic Techniques.** 18 Cat 1 Credits. Info: Lisa Krehbiel, Institute for Medical Studies, 30131 Town Center Dr, Suite 215, Laguna Niguel, CA 92677. Tel: (714) 495-4499.

ILLINOIS

Oct 16–17. **Perinatal Medicine 1986—Back to Basics.** Cat 1 Credits (13 hours). *Oct 20–24.* **Doppler Echocardiography Workshop.** Cat 1 Credits (33 hours). Info: Paula Puntenney, Alumni Center for Continuing Education, Northwestern University Medical School, 301 East Chicago Ave, Chicago, IL 60611. Tel: (312) 908-8533.

KANSAS

Oct 15–18. **Group Psychotherapy.** 20 Cat 1 Credits. Seeley Conference Center, The Menninger Foundation, Topeka. Info: Jane Bolte, Conference Coordinator, Division of Continuing Education, The Menninger Foundation, Box 829, Topeka, KS 66601. Tel: (913) 273-7500 Ext 5992.

(*continued on p 13A*)

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COMMENTARIES

On smoking and drinking and crashing

Although the studies have been few, they have been quite consistent; cigarette smokers have higher rates of highway crashes than do nonsmokers. This observation is again verified in the paper by DiFranza et al published in this issue of the *Journal*.[1] The unanswered question, however, is why this relationship exists.

Early researchers attributed a higher crash experience to the fact that smokers may be distracted while "lighting up," searching for an ashtray, or seeking to extinguish a stray ember. One psychologist noted that smokers are orally dependent and identified this trait as the underlying culprit.[2] The work of DiFranza et al and our own research,[3] however, have focused on a different connection; heavy drinkers tend to be heavy smokers, and the relationship between alcohol consumption and highway crashes is copiously documented.

At a blood alcohol concentration (BAC) above 0.05% by weight, crash risk rises rapidly. It is about three times that of the nondrinker at 0.08%, rising to six to eight times at 0.10% and to over 25 times at 0.15%.[4] Among teenagers the crash risk increases with even one drink and at higher BACs rises even more rapidly than for older persons. Furthermore, the more severe the crash, the greater the likelihood that alcohol is involved and that the BAC is substantially above 0.10%. This marked association between alcohol consumption and injury severity reflects not only the increased likelihood of getting into a crash, but also the fact that alcohol acting at intercellular and intracellular levels appears to heighten the sensitivity of neural and other tissues to severe damage upon only modest impact.[5]

Our own work and that of others has shown that, at least among men, most heavy drinkers are smokers and they tend to be heavy smokers.[3,6] Other studies indicate that alcoholics overwhelmingly are heavy smokers.[7,8] The question raised by DiFranza and associates, therefore, is whether the apparent association between smoking and crashing is entirely a reflection of this third variable, the drinking connection. Their answer clearly is no. Among heavy drinkers who were nonsmokers, 22% reported involvement in one or more crashes, and 23% noted having received one or more citations for moving violations. Twenty-five percent of heavy drinkers who were smokers, however, reported crashes and 29% had records of violations. Thus relative risks among smokers were 1.16 and 1.28 respectively for crashes and violations.

But questions still remain because of the design of the research. Do smokers who are heavy drinkers have higher crash and violation rates than the nonsmoking drinkers because of the physiological and other effects of the smoking per se or because of yet other characteristics that are associated with the smoking? It has been reported that the impairment of vision caused by a somewhat elevated carboxyhemaglobin (COHb) level is equivalent to the effects of one or two drinks of alcohol, but, as noted by DiFranza and his colleagues, it is also known that smokers tend to take risks not only in smoking but in other areas of their lives as well. It may be that heavy drinkers who are also smokers express even more of this devil-may-care attitude than do those who are heavy drinkers only.

Our own research attempted to examine the smoking-drinking association in specific crashes, rather than examining the crash association among specific types of persons. We compared proportions of Vermont driver fatalities and interviewed site-time matched drivers not involved in crashes in terms of recent alcohol consumption (BAC $\geqslant$ 0.02%) or cigarette smoking only, both, or neither. (Among fatalities a COHb of 5–15% was considered to indicate recent smoking in crashes not involving fire.)

Relative risks (RR) of being a fatality were as follows: no smoking, BAC $<$ 0.02%: RR = 1.00; smoking only: RR = 3.16; BAC 0.02–0.09%: RR = 1.79; smoking plus BAC 0.02–0.09%: RR = 3.75; BAC $\geqslant$ 0.10%: RR = 40.66; smoking plus BAC $\geqslant$ 0.10%: RR = 48.66. At BACs below 0.10% smokers are significantly over-represented compared to those with no alcohol or with alcohol only ($p <$ .05 at BAC $<$ 0.02%, $p <$ .10 at BAC 0.02–0.10%). At BACs of 0.10% or higher, smokers are apparently, but not significantly, overrepresented in this study compared to those with alcohol only ($p >$ .40), presumably either because alcohol becomes such an overriding factor or because sample size of non-crash-involved drivers was quite small at higher BACs. Conceivably with a larger sample

size statistical significance might have been achieved at higher BACs as well.

Since both blood loss and facial or chest injury with relative hypoxia are common problems in crashes, however, it is not possible based on this study to determine whether the overrepresentation of smokers (as measured by COHb) among the fatalities reflects a greater likelihood of crashing, of fatal outcome because of compromised oxygenation caused by the smoking, or both. That question still needs to be answered through research involving drivers in nonfatal crashes and site-time matched controls.

With respect to emergency care, it is obvious that emergency medical technicians (EMTs) and physicians who treat people injured in crashes or sustaining other injuries after drinking must assume that they are dealing not only with facial and/or chest injury and blood loss but with altered oxygenation as well because of the probable presence of an elevated COHb, perhaps also accompanied by respiratory disease. A greater willingness to administer oxygen to the victim while enroute to the hospital may in some cases provide enough of a margin of safety to prevent death or permanent brain damage from relative hypoxia.

The relevance of the smoking and drinking connection, of course, extends considerably beyond the question of highway safety. Alcoholism has increasingly been recognized as a problem of multisubstance abuse, and the addiction to cigarettes commonly remains long after the addiction to alcohol has been controlled, suggesting that the former addiction may be even more virulent than the latter. Meetings of Alcoholics Anonymous almost invariably are pervaded by the acrid gray haze of cigarette smoke, although in recent years a few chapters of AA have been established with the intention of helping members to cope with both addictions.

Physicians commonly breathe a sigh of relief if they are able to deal effectively with alcohol abuse, but they often regard tobacco abuse as a lesser evil that they are willing to accept as incurable. I think it is time to ask whether this relative incurability is a fact, or simply an attitude that defeats us before we begin. The drinking and smoking combination (which has been recognized by the tobacco companies that also own companies producing alcoholic beverages) deserves far more attention—both in the form of epidemiologic, psychological, and laboratory research, and in well evaluated intervention programs to prevent the dual addictions and to attain dual recovery.

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Smoking control: A consumer issue

Safe products are a first priority for consumer groups worldwide. By carefully testing the quality of goods and services, comparing prices, and reporting their findings in their publications, consumer organizations do their best to see that consumers obtain full and frank information and the best value for their money. Consumers have a right to fair and honest trade practices, standard levels of quality, product safety and performance, and information on which to base their choices.

The International Organization of Consumers Unions (IOCU) links the activities of consumer organizations in some 50 countries. It coordinates their skills and expertise and provides support for recently formed consumer groups, particularly in countries where the consumer movement is itself relatively new. IOCU undertakes research and action, arguing the consumer case internationally on issues of concern to consumers worldwide.

The main issues for consumer organizations around the world have found their expression in the seven consumer rights: the right to safety, the right to choose, the right to be informed, the right to redress, the right to a healthy environment, the right to be heard, and the right to consumer education.

When these rights are violated, consumer organizations and the IOCU are ready to undertake action and launch campaigns. One such campaign was launched at the IOCU's 11th World Congress. There the IOCU and its members decided that a worldwide campaign to oppose tobacco advertising and sponsorship should become a major focus for the consumer movement.[1]

Since the 1960s, health and medical organizations have been active in publicizing the health consequences of smoking. Those efforts are concentrated mainly on the individual smoker, while the tobacco industry proceeds with its billion dollar advertising and promotional activities.

Monitoring the industry's promotional activities and supporting local action and international advocacy, the IOCU opposes this industry and campaigns for a ban on all forms of tobacco advertising and sponsorship.

The promotion of a product that has no accepted safe level of use is an abuse to consumers. The IOCU tobacco campaign challenges the right of the tobacco industry to promote its products and to persuade nonsmokers to take up the habit.

Each year more than one million people die from diseases caused by smoking. If any other product were implicated in as many deaths as tobacco, it would have to be made safe or it would be ordered off the market, as has happened with other products once their hazardous nature has been established. Tobacco is the single most hazardous product on sale and the only advertised product which is hazardous when used as intended.[2]

The use of tobacco violates the seven consumer rights.

The *right to safety* is a first and prime consumer right. Safety is the sense of assurance that the products we consume are not harmful. The ill effects of smoking are no longer questioned.

As the World Health Organization's Executive Board stated at its meeting in January 1986: "Cigarette smoking is the major avoidable cause of ill health and premature mortality in countries where it is widespread," and, "to suggest priority for continuing basic research further to prove the causal relationship between disease and tobacco would simply buy time for adverse commercial interest." [3] Tobacco kills, and the only safe cigarette is an unlit one.

Consumers also have a *right to choose*, which means selecting from a variety of goods at competing prices. Tobacco advertisements promote the idea that smoking is a normal and good thing to do. Young people especially are persuaded that smoking is very desirable. As the Royal College of Physicians has stated in its report, *Smoking or Health* (London, 1978): "Learning to smoke usually occurs in childhood or adolescence. The matter is largely settled by the age of 20; if a person is still a nonsmoker at that age, he is unlikely to take it up." [4] Even now that the scientific evidence about the dangers of tobacco use is overwhelming, people still continue to smoke. People continue with this habit because smoking is addictive. Many smokers either wish to or have tried to give up smoking. For an addicted tobacco user a free choice does not exist any more.

A possibly even more serious violation of the right to choose is related to the nonsmoker. The nonsmoker is forced to breathe the polluted air at his or her work and in many public places. As research points out, tobacco smoke inhaled by passive smokers contains the same carcinogens as the smoke inhaled by active smokers.[5,6] Studies from the World Health Organization show that there is three times as much tar, nicotine, and other chemicals in side stream smoke as in main stream smoke.[7] Passive smoking constitutes a true health hazard and is therefore of public health concern.

Incorporated in the right to choose is the right to have basic needs met. Consumers should have access to the goods and services they need such as food, clothing, and transport. The tobacco industry, with its declining market in the developed world, has found a new market among the poor people of the developing world. With the perception of bringing an "affordable luxury to the poor," the tobacco industry has launched advertising campaigns in developing countries where cigarettes are associated with prestige, power, freedom, and luxury. The lessened ability to buy food as the poor smoker spends part of his marginal survival income on cigarettes has indirect health effects on him and his family.[8]

The *right to fair and honest information* means the right to be given facts needed to make an informed choice or decision. The right to be informed goes beyond the avoidance of deception and protection against misleading advertising, labelling, or other practices. Cigarettes contain many chemicals, including a wide range of pesticides, synthetic flavorings, and other chemical agents. Most countries do not have regulations that limit the tolerance for pesticide residues in the cigarettes they import. And in many cases no regulations exist to control the quality of tobacco to satisfy health standards regarding contents. No consumer organization is willing to accept this lack of standards in other products made for consumption.

Another important right is the *right to redress*. This means the right to a fair settlement of just claims. The tobacco industry, being internationally well organized, has been able to retain the right to promote its products through strong, persistent, and effective lobbying. The industry is the largest, most determined, and most effective source of opposition to worldwide efforts to reduce smoking. So far no court has held the tobacco industry responsible for any death or disease due to smoking, or for the resultant yearly costs in health care, loss of jobs, or damage by fire. Consumers are denied any redress from the tobacco companies which sell products that contain a major threat to public health.

Consumers also have a *right to a healthy environment*. This right involves protection against environmental problems over which the individual has no control. In poor countries and those without coal deposits, wood is the main fuel used for tobacco curing. Tree felling in the developing countries for the curing of tobacco accounts for 3.9% of annual total world deforestation[9] (which also has effects on climate). Where tobacco is grown in hilly areas, soil erosion is common. In addition, the production of tobacco competes with the production of food. Tobacco companies prefer to buy tobacco from their own farmers rather than on the open market. They have developed extensive agricultural schemes in which they give massive support to farmers. Other crops cannot compete, and many farmers then turn to tobacco farming rather than food production.

The *right to be heard* means the right to be represented so that consumers' interests receive full consideration in the formulation and execution of economic policy. If tobacco were invented in a laboratory today, given all the currently available information, no government would allow it to be sold.

But governments are not the first to climb barricades to introduce smoking control measures. A strong tobacco lobby that fights for the interests of farmers and employees also influences governments to value the short term benefits of tobacco profits above the long term social and economic costs to society. However, some governments

(especially in the Nordic countries) are fully aware that their responsibility is to protect health and they have introduced smoking control measures.

Consumer education is the right to acquire the knowledge and skills to be an informed consumer throughout life. Cigarettes are one of the most heavily promoted products in the world. Billions of dollars are spent to keep people smoking and to attract nonsmokers to the habit. The tobacco industry itself is not telling its buyers the consequences of their purchase. Thus, government commitment and an educational infrastructure are needed for health education. In developing countries the only channels open to health educators for spreading antismoking messages are schools and primary health contacts.

Smoking has been regarded by many as primarily a medical problem. As a consequence, most measures to combat smoking have been aimed at individuals, rather than at the real cause of the problem—the tobacco industry. Tobacco multinationals frustrate and dissuade governments from enacting any form of tobacco legislation. The tobacco industry ignores voluntary agreements on the promotion of cigarettes, and uses different standards in the marketing strategies for developing and developed countries.

Through information, education, testing, lobbying, and applying pressure, the IOCU, its members, and like minded groups the world over are trying to increase the awareness of consumers to encourage them to fight for their rights. In the case of tobacco products we have outlined how these rights are being violated. There is no case for allowing unrestricted promotion of tobacco products.

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CONSULTING EDITORS OF THE *JOURNAL*

John T. Flynn, MD

John T. Flynn, MD, has been Consulting Editor at the *New York State Journal of Medicine* since 1983. Following graduation from Cornell University Medical College in 1942 and an internship in internal medicine at the New York Hospital, he served for three years on the staff of the 56th US Army General Hospital in England, Normandy, and Belgium, and later, as Chief Medical Officer of the Port of Marseilles.

On returning to the United States, Dr Flynn completed his residency training in internal medicine on the 2nd (Cornell) Medical Division at Bellevue Hospital in New York City. After two years as a Commonwealth Fellow in Internal Medicine at New York Hospital, he joined the full-time faculty of Western Reserve University School of Medicine, where he taught and conducted research for four years.

Entering private practice in New York City in 1955, Dr Flynn rejoined the staff of the New York Hospital. For many years, he served as a medical consultant to major corporations, and has held several directorships in the banking, insurance, and amusement industries. A lifelong interest in aviation and experience as an aircraft pilot led Dr Flynn to consulting work for the Federal Aviation Agency in establishing physical standards for private and commercial pilots. As contributing editor of *Flying Magazine*, he authored many articles on the medical aspects of aviation piloting.

After becoming Chief of Medicine at the Beekman Downtown Hospital in 1965, Dr. Flynn edited more than 60 clinical pathological conferences (CPCs) held in his department for the *New York State Journal of Medicine*. Since 1983, he has continued his CPC contributions to the *Journal*. For his contributions to the *Journal* over the years, Dr Flynn received the Redway Award of the Medical Society of the State of New York in 1985. Since 1980, Dr Flynn has been senior Medical Editor of the Video Clinic Program of the American Medical Association, and currently is re-editing these medical television programs for cablecast.

Dr Flynn is currently Associate Chief of Medicine at New York Infirmary-Beekman Downtown Hospital.

Dr Flynn is a member of the Alpha Omega Alpha Honorary Society, a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, and Associate Professor of Clinical Medicine at his alma mater, Cornell University Medical College. Over many years as a Fellow of the New York Academy of Medicine, his past and current activities have included the offices of Vice President, Trustee, and Council member, and membership on the Committee on Public Health for which he has chaired numerous subcommittees.

Dr Flynn is currently developing a series of clinical case conferences for regular publication in the *Journal* which will emphasize the practical aspects of patient management.

Carl Pochedly, MD

When Carl Pochedly entered Hiram College in northern Ohio he chose English as his major and dreamed of writing the "Great American Novel." He had been class poet and editor of his rural high school newspaper. He soon switched his major to premed, but a battle raged within him between the desire to write and the desire to study medicine. While in medical school at Case Western Reserve University, he dabbled in writing fiction and sometimes neglected his studies. His hero was Somerset Maugham, the novelist who had been a physician. Dr Pochedly earned his MD degree in 1956, but the conflict between literature and medicine was not resolved for many years.

After residency training in pediatrics at Children's Hospital in Washington, DC, and a fellowship in pediatric hematology at New York Medical College, Dr Pochedly joined the full-time staff at Nassau County Medical Center in 1967. He soon became involved in writing in his specialty and produced a profusion of case reports, reviews, and clinical research articles. He then went on to write and edit a rapidly growing list of books and monographs. In 1979, after seeking a publisher for three years, he founded the *American Journal of Pediatric Hematology/Oncology* and became the editor.

Dr Pochedly was Professor of Clinical Pediatrics at the School of Medicine, State University of New York at Stony Brook. In addition to directing an in-patient service and clinic for children with cancer and blood diseases, he has authored over 130 scientific articles and has published 16 books dealing with various aspects of childhood cancer. His books include *Neuroblastoma: Clinical and Biological Manifestations* (1982); *Wilm's Tumor* (1984), co-authored with E. S. Baum; *Childhood Lymphoblastic Leukemia* (1985); *Non-Lymphoid Leukemia in Children* (1985); and *Human Values in Pediatric Hematology/Oncology* (1986). He is a member of the editorial board of *Critical Review in Oncology/Hematology*.

Dr Pochedly serves as secretary/treasurer of the American Society of Pediatric Hematology/Oncology, whose founding he promoted in 1981. He is a member of the American Academy of Pediatrics, the American Association of Hematology, and the American Association for Cancer Research. In 1985 he became Director of Pediatric Hematology/Oncology and Academic Research at T. C. Thompson Children's Hospital in Chattanooga, Tennessee. Dr Pochedly has been editing the "Essays in Pediatrics" section of the *Journal* since 1985.

Richard B. Birrer, MD

Richard Birrer received his MD degree from Cornell University Medical College in 1975. Thereafter he did his internship in family practice at the Hunterdon Medical Center in Flemington, New Jersey. From 1977 to 1979 he voluntarily served as a family physician (Captain) in the United States Air Force in Athens, Greece. He received the Meritorious Service Medal for his efforts in health care and education. Dr Birrer completed his training in family practice at the State University of New York Health Science Center at Brooklyn from 1979 to 1981. During his year as Chief Resident he was a recipient of the Parke-Davis Teacher Development Award in Family Medicine.

In 1982 he received a Master of Public Health degree in international health policy from the Harvard University School of Public Health. Thereafter he became Director of Medical Services at the East New York Neighborhood Family Care Center.

In the latter part of 1983 Dr Birrer assumed his current position as Director of Undergraduate Education and Associate Director of Family Practice at SUNY Health Science Center at Brooklyn. He was awarded a $225,000 Department of Health grant for the development of a community based school health project in the East New York section of Brooklyn. He was a Senior Fulbright Scholar in 1984, during which time he taught the principles and practice of family practice in Egypt. Dr Birrer was recently promoted to Associate Professor of Family Practice. He will serve in the Health Scientist Exchange to the USSR under the Fogarty program later this year.

Dr Birrer is the author of over 100 peer reviewed articles and monographs and several textbooks. He is an active member of the American Medical Association, the American College of Sports Medicine, the Society of Teachers of Family Medicine, and the American Academy of Family Practice. He is a Diplomate and Fellow of the American Boards of Family Practice and Emergency Medicine.

The relationship of smoking to motor vehicle accidents and traffic violations

JOSEPH R. DIFRANZA, MD; THOMAS H. WINTERS, MD; ROBERT J. GOLDBERG, PHD; LEONARD CIRILLO, PHD; TIMOTHY BILIOURIS

ABSTRACT. Differences between smokers and nonsmokers in the frequency of motor vehicle accidents and traffic violations were examined in two populations. Self-administered questionnaires were used to collect data on these outcomes as well as on smoking habits, drinking habits, age, gender, marital status, education, years of driving experience, and number of miles driven annually. Smokers had 50% more traffic accidents and 46% more violations than nonsmokers. The excess of accidents and violations among smokers remained when differences in alcohol consumption, age, driving experience, and education were taken into account, and may reflect in part more frequent risk taking behavior among smokers.

(NY State J Med 1986; 86:464-467)

Smokers have been reported to be involved in motor vehicle accidents at a rate higher than that of nonsmokers.[1,2] Differences between smokers and nonsmokers in alcohol consumption and driving style may in part be responsible. The present study seeks to determine if (1) smokers are at increased risk of having accidents, (2) drinking accounts for the association of smoking and accidents, and (3) differences in driving styles between smokers and nonsmokers are reflected in an excess of traffic violations among smokers. Differences between smokers and nonsmokers in the frequency of accidents and traffic violations are studied in two populations.

METHODS

This cross-sectional study of smoking, motor vehicle accidents, and traffic violations was carried out among two population samples in Worcester County, Massachusetts, between March and December, 1984.

Population I—Probation Alternative Traffic School (PATS). This population was selected to examine the relation of smoking to accidents because of the relative infrequency of accidents among the general driving population. Drivers receiving traffic tickets for minor violations in Worcester and surrounding communities are given the option of attending a three-hour traffic safety course in exchange for having the violation annulled. Excluded are drivers stopped for drunken driving and those who receive a ticket as a result of an accident. All drivers attending PATS over a four-month period were asked to complete a self-administered questionnaire. The response rate was greater than 95%, resulting in 1,715 completed questionnaires.

Population II—Registry of Motor Vehicles. To study the relationship of smoking to traffic violations, drivers applying for license renewals at the Registry of Motor Vehicles were asked to complete a questionnaire. (Drivers must renew their licenses in person every four years.) To ensure anonymity at this location, a padlocked ballot box was provided for the completed questionnaires. Participation was 90%, with 1,999 usable questionnaires returned.

A brief self-administered questionnaire was given to all study participants. Subjects were asked to report the number of traffic accidents and moving violations they had had during the preceding year. Additional questions were asked concerning their smoking habits, drinking habits, age, gender, marital status, education, years of driving experience, and number of miles driven annually.

A smoker was defined as a person who had regularly smoked cigarettes at any time during the preceding year. Traffic violations included only moving violations.

Differences in the distribution of selected characteristics were examined using chi square and t-tests for discrete and continuous variables respectively. The Mantel-Haenszel measure of relative risk was used to analyze the data presented in Tables III and VII. This test computes a summary measure of the relative risk adjusted for potential confounding factors.

Prior to chi square analysis, each of the variables other than smoking and driving record was retrospectively dichotomized in such a way as to maximize the strength of the association of that variable with driving record and still obtain an adequate number of cases in each group.

TABLE I. Relationship of Cigarette Smoking to Accident Record—Population I

	0 Accidents	1 Accident	% Having Had One or More Accidents
Smokers	481	134	21.8
Nonsmokers	911	160	14.9

From the Departments of Family and Community Medicine (Dr DiFranza) and Medicine and Epidemiology (Dr Goldberg), University of Massachusetts Medical Center; Clinical Medicine, Boston University School of Medicine (Dr Winters); Psychology, Clark University (Dr Cirillo); and University of Massachusetts Medical School (Mr Biliouris).

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TABLE II. Differences in Selected Characteristics Between Smokers and Nonsmokers—Population I

	Nonsmokers	Smokers	p Value*
Average age†	32.3	31.0	0.001
Average years of driving experience†	15.1	13.9	0.001
% Married†	44.8	41.0	NS‡
% Males†	67.7	65.2	NS‡
% College graduates†	52.1	36.1	0.0001
% Drinking >10 drinks per week†	14.2	21.9	0.0001

* Calculated by t-test or chi square analysis.
† Variables related to accident record at $p < 0.01$.
‡ Not significant.

Results

Population I. In the PATS study group, smokers as compared to nonsmokers had a relative risk of 1.46 of being involved in one or more accidents during the preceding year (corrected chi square = 12.3, df=1, $p < 0.0005$; Table I). Smokers had a total of 50% more accidents than nonsmokers.

Individuals involved in accidents differed from accident free drivers in being younger, having had fewer years of driving experience, being less educated, and consuming more alcohol ($p < 0.01$ by chi square analysis or t-test for each comparison). Smokers differed significantly from nonsmokers in being younger, being less experienced drivers, being less educated, and being heavier drinkers ($p < 0.001$ by chi square or t-test; Table II).

The four variables related to both smoking status and accident record were considered as potentially confounding factors and were examined in subsequent stratified analysis. As seen in Table III, smokers had a relative risk greater than one in each subgroup. Mantel-Haenszel analysis failed to reveal any significant heterogeneity of the relative risk across any of these variables.

The largest difference in accident rates between smokers and nonsmokers was seen among those who stated that they never drink alcoholic beverages. In this group, smokers were 2.18 times more likely to have been involved in one or more accidents during the preceding year ($X^2 = 8.53$, df=1, $p < 0.005$; Table IV).

Population II. Smokers in the Registry group had a relative risk of 1.25 of having incurred one or more traffic violations during the preceding year ($X^2 = 4.25$, df=1, $p < 0.05$; Table V). Smokers had received a total of 46% more tickets than the nonsmokers.

Smokers in the Registry group differed from the nonsmokers in being younger, having fewer years of driving experience, being less educated, and being heavier drinkers ($p < 0.001$ by chi square and t-test; Table VI). The variables age, driving experience, and alcohol consumption were also related to violation record, with drivers who were younger, less experienced, or heavier drinkers receiving more violations ($p < 0.001$ by chi square and t-test).

The variables age, driving experience, and alcohol consumption were each dichotomized and the percentages of smokers and nonsmokers who had received tickets were examined in each subgroup. As seen in Table VII, an excess of violations among smokers was observed in each subgroup. Mantel-Haenszel analysis failed to reveal any significant heterogeneity of the relative risk across any of these three variables.

The PATS group differed from the Registry group in having more male members, being younger, less often married, driving more miles annually, drinking more, and having fewer years of driving experience.

Discussion

Among a group of drivers stopped for traffic violations, smokers were found to have had 50% more accidents than nonsmokers. This result is in close agreement with a prior study which showed a 40% excess of accidents among Air Force recruits who smoked.[2] These findings are also consistent with insurance data which reveal that smokers make 24% more claims against their auto insurance policies (personal communication, The Hanover Insurance Companies). The excess of accidents among smokers cannot be attributed solely to differences between smokers and nonsmokers in age, driving experience, education, gender, marital status, or number of miles driven annually. Rather, a combination of other factors appears to be responsible for the association of smoking and motor vehicle accidents.

The heavier use of alcohol by smokers undoubtedly plays a major role.[3] Smokers are arrested for drunken driving at a rate 3.4 times that for nonsmokers.[4]

However, higher accident rates for smokers were seen both among teetotalers and among drinkers matched for their level of alcohol consumption. Therefore, alcohol use does not completely explain the association of smoking and accidents.

Since we were unable to verify the actual drinking behavior of our subjects it is possible that despite the prom-

TABLE III. Accident Rates of Nonsmokers and Smokers Within the Described Subgroups

Subgroup	Percentage Having Had One or More Accidents: Nonsmokers	Percentage Having Had One or More Accidents: Smokers	Relative Risk*	Estimate of Relative Risk for Both Subgroups Combined†
Under 30 years old	19.3	26.9	1.39	1.56
Aged 30 or older	10.2	15.3	1.50	
<13 Years' driving experience	18.4	26.6	1.45	1.58
≥13 Years' driving experience	10.6	15.3	1.44	
No college degree	17.4	23.5	1.35	1.52
College graduate	12.7	18.8	1.48	
<10 Drinks per week	13.9	20.8	1.50	1.52
≥10 Drinks per week	21.9	25.4	1.16	

* Relative risk of having one or more accidents: smokers/nonsmokers.
† Mantel-Haenszel estimate.

TABLE IV. Relationship of Cigarette Smoking to Accident Record Among Teetotalers—Population I

	0 Accidents	1 Accident	% Having Had One or More Accidents
Smokers	73	24	24
Nonsmokers	198	25	11

ise of anonymity some individuals understated their drinking habits. Since smokers drink more heavily, such dishonesty would cause an underestimation of the role of alcohol in smoking related accidents.

Smokers as a group differ from nonsmokers in certain personality traits that influence driving behavior. Previous research has demonstrated several personality characteristics that are more common among individuals who smoke (F. L. McGuire, unpublished data, 1980). Those characteristics—impulsivity, immaturity, extroversion, sociopathy, and poor mental health—are also more common among individuals who are frequently involved in motor vehicle accidents.[5-7] The common denominator here may be the willingness to take risks.

Smokers have been shown to take more risks than nonsmokers. Smoking itself entails considerable risk of illness and death. Smokers are also more willing to risk injury or death by not wearing seat belts.[8] In addition, they have been shown to take health risks in more passive ways by less frequently having general physical exams, dental checkups, Pap smears, and immunizations.[9,10]

It is a reasonable expectation, then, that smokers might also be more willing to take risks in certain driving situations. Many traffic violations, such as speeding and failing to stop for a red light (which made up the majority of violations in this study), commonly result from taking calculated risks and are easily avoided by the cautious driver. In this study, traffic violations were used as an indicator of risk-taking driving behavior. Smokers incurred 46% more traffic violations than nonsmokers, lending support to the theory that smokers have more accidents in part because they take more risks while driving.

One previous study attempted to measure differences in risk taking between smokers and nonsmokers using a forerunner of the arcade auto race games.[11] Participants were offered cash prizes for the fastest time. Under these conditions, when the rewards for speeding were real and the dangers were not, there were no differences between smokers and nonsmokers in the willingness to take risks. We do not consider these results to be applicable to real life driving.

Although not specifically addressed by the present study, brief mention should be made of other factors that may contribute to excess accidents among smokers: distraction, drug abuse, and the physiologic effects of smoking. The degree to which any of these factors contribute is presently unknown.

TABLE V. Relationship of Cigarette Smoking to Violation Record—Population II

	0 Tickets	≥1 Tickets	% With One or More Tickets
Smokers	581	130	18.3
Nonsmokers	1,074	184	14.6

TABLE VI. Differences in Selected Characteristics Between Smokers and Nonsmokers—Population II

	Nonsmokers	Smokers	p Value*
Average age†	40.5	36.9	0.001
Average years of driving experience†	21.8	18.7	0.001
% Married†	63.2	59.9	NS‡
% Male†	47.6	47.2	NS‡
% College graduates	51.1	37.1	0.0001
% Drinking >10 drinks per week†	9.5	16.5	0.0001

* Calculated by t-test or chi square analysis.
† Variables related to violation record at $p < 0.001$.
‡ Not significant.

A momentary distraction at a critical moment could result in a collision. Eighty-eight percent of the smokers in our pilot study reported that they smoke while driving. When tested on a monotonous simulated driving test smokers showed only a statistically nonsignificant deterioration in performance while smoking.[12] However, our interviews with smokers have produced many descriptions of collisions due to the manipulation of cigarettes, especially the dropping of burning embers. Distractions due to smoking are definitely a factor in some accidents and may play an even greater role in accidents involving drivers already impaired by the influence of alcohol or drugs.

The degree to which illegal drug use contributes to accidents is unknown.[13] Smokers are twice as likely as nonsmokers to experiment with illegal drugs, thus drug use may contribute to the excess of accidents among smokers.[14] However, because self-reports regarding drug use are unreliable, drug use was not addressed by this study.

Carbon monoxide and nicotine, two physiologically active components of cigarette smoke, could theoretically have adverse effects on driving ability. The effects of acute exposure to carbon monoxide on the following driving related functions have been studied: reaction time, depth perception, visual acuity, dark adaptation, recovery of dark adaptation following exposure to glare, auditory and visual vigilance, velocity estimation, and eye-hand coordination.[15-17] At the levels of carbon monoxide exposure that are common with smoking, these studies have produced conflicting results. Two factors further complicate the interpretation of these results. It is possible that due to compensatory elevations of hemoglobin the same effects might not occur as a result of chronic exposure from smoking.[17] Also, the stimulant effects of nicotine may counteract some of the depressant effects of carbon monoxide.

The only likely effect of smoking on a driving related physiologic function is a reduction of visual thresholds with resultant poorer night vision.[16,17] A recent study demonstrated that smokers have a higher proportion of their accidents at night.[19] Although this finding may have been attributable to decreased night vision, it may also have been due to alcohol consumption.

TABLE VII. Violation Rates of Smokers and Nonsmokers Within the Described Subgroups

Subgroup	Percentage Having Had One or More Violations: Nonsmokers	Percentage Having Had One or More Violations: Smokers	Relative Risk*	Estimate of Relative Risk for Both Subgroups Combined†
Under 30 years old	25.3	26.3	1.04	1.23
Aged 30 or older	9.4	13.3	1.41	
<13 Years' driving experience	23.9	24.8	1.04	1.22
≥13 Years' driving experience	8.9	13.0	1.46	
<10 Drinks per week	13.6	16.1	1.18	1.25
≥10 Drinks per week	22.9	29.3	1.28	

* Relative risk of having a violation: smokers/nonsmokers.
† Mantel-Haenszel estimate.

Other studies have attempted to examine the effects of smoking on the performance of specific driving related tasks. Due to poor experimental design, however, most have unwittingly studied the effects of nicotine withdrawal.[20,21] Not surprisingly, nicotine withdrawal causes a deterioration in driving skills.[12] However, when smokers and nonsmokers were compared in the laboratory setting, no significant differences in driving skills were evident.[12,22]

This study identifies people who smoke cigarettes as being at increased risk of being involved in motor vehicle accidents and traffic violations as compared to nonsmokers. The higher accident rate seen among smokers can be attributed to greater risk-taking behavior, more frequent use of alcohol and illegal drugs, and less attentive driving due to the physical distractions involved with smoking. Physiologic effects of cigarette smoke may possibly play a minor role.

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Smoking and health in Czechoslovakia

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In Czechoslovakia, as in other countries, medical workers are the first persons to encounter smoking related diseases. Physicians were among the first to take strong action against smoking. The Scientific Expert Committee of the Czech Medical Association published a proclamation in 1976 stating its opinion on the then current medical evidence concerning the health hazards of smoking and suggesting preventive measures. The recommendations included legislative action to support the control of smoking, public education and information aimed especially at young people and women, and specific actions to promote the cessation of smoking.

The following epidemiologic data gives a clear picture of smoking habits in Czechoslovakia and the health consequences of smoking.

PREVALENCE OF SMOKING AND CONSUMPTION OF CIGARETTES

In 1983, a study was carried out in seven districts, representing the population of the Czech Socialist Republic (CSR), within the framework of the Integrated Programme for the Prevention of Non-Infectious Diseases (IPP study). A random sample of 1,054 men and 999 women representing three age groups (25–29, 40–44, and 55–59 years of age) replied to a questionnaire on their smoking habits and daily cigarette consumption.[1]

The highest proportion of cigarette smokers was found among men and women in the age group 25–29 years of age, accounting for 55.3% and 41.9%, respectively (Table I). With increasing age, the proportion of smokers diminishes to 32.0% and 12.1%, respectively, while the proportion of male ex-smokers increases to 33.9%, and that of female smokers remains constant at about 10%.

The average number of cigarettes smoked daily by current smokers is highest among men (Table II). More than half of the men currently smoking consume 11 to 20 cigarettes daily, while two thirds of women smokers smoke ten or fewer cigarettes daily. The proportion of heavy smokers, who consume 21 or more cigarettes per day, tends to increase with age in both sex groups.

The IPP study yielded data on smoking habits of children aged 12–14 years.[2] Of 941 children selected at random in the same districts of the CSR, 5.1% (0.7–13.1)* had smoked for the first time before the age of six years; 10.5% (5.2–17.4) from 7 to 8 years of age; 13.6% (8.2–20.2) from 9 to 10 years; 14.1% (8.7–20.7) from 11 to 12 years, and 3.5% (0.1–12.5) at the age of 13 years or later. Of the children who tried to smoke, 89% (65.6–91.9) smoked only once or twice, and 10% (2.9–20.7) became occasional smokers. The rest became regular smokers.

Per capita consumption of cigarettes manufactured in the CSR increased from 1,384 in 1955 to 1,853 in 1982—an increase of 24%. Per capita consumption peaked in 1978 at 1,961 cigarettes.

TABLE I. Proportion of Nonsmokers, Ex-smokers, and Current Smokers, IPP Study, 1983 (N = 2,053)

Age (yr)	Smoking Habit	Proportion in Men	Proportion in Women
25–29	Nonsmokers	30.9 (26.6–35.6)*	48.1 (42.9–53.1)
	Ex-smokers	13.8 (10.8–17.6)	10.0 (7.2–13.4)
	Current smokers	55.3 (50.1–59.8)	41.9 (37.0–47.1)
40–44	Nonsmokers	30.7 (26.0–36.3)	64.1 (58.4–69.4)
	Ex-smokers	19.8 (15.7–24.7)	11.0 (7.7–14.8)
	Current smokers	49.5 (43.6–54.6)	24.9 (20.2–30.1)
55–59	Nonsmokers	24.1 (28.8–39.4)	78.8 (74.3–83.4)
	Ex-smokers	33.9 (28.8–39.3)	9.0 (6.1–12.5)
	Current smokers	32.0 (26.9–37.3)	12.1 (8.6–15.9)

* Confidence interval.

LUNG CANCER

Age-specific incidence rates of lung cancer in Czechoslovakia, determined on the basis of reported cases, in-

TABLE II. Proportion of Current Smokers According to Sex and Age Compared with the Average Number of Cigarettes Smoked Daily, IPP Study, 1983 (N = 755)

Age (yr)	Daily Cigarette Consumption	Proportion in Men	Proportion in Women
25–29	<10	41 (34.6–47.6)*	78 (71.1–84.2)
	11–20	51 (44.4–57.6)	21 (14.9–27.8)
	>21	8 (4.8–12.0)	1 (0.1–3.3)
40–44	<10	28 (21.2–35.4)	66 (54.8–76.3)
	11–20	53 (45.1–60.8)	33 (22.3–44.1)
	>21	19 (13.2–25.6)	1 (0–4.5)
55–59	<10	32 (23.2–41.4)	68 (52.3–81.8)
	11–20	47 (37.3–56.8)	29 (15.7–44.4)
	>21	21 (13.6–29.5)	3 (1.4–5.2)

* Confidence interval.

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* Confidence intervals are calculated using the following transformation: 2 (arcsin $\sqrt{p}$)

TABLE III. Age-specific Incidence Rates for Lung Cancer on the Basis of Reported Cases, by Sex and Age, Czechoslovakia, 1970–1984.

Age	1970	1975	1980	1984
Men				
25–34	1.5*	2.1	1.8	1.8
35–44	16.5	21.1	20.7	23.9
45–54	70.0	102.3	118.3	138.0
55–64	230.6	259.1	266.5	260.6
65–74	458.7	480.4	365.7	461.0
75 +	333.8	466.1	603.0	571.3
Women				
25–34	0.7	0.4	0.8	0.6
35–44	2.1	3.9	3.5	3.1
45–54	7.0	8.6	9.2	11.3
55–64	15.8	26.1	20.6	32.8
65–74	31.1	30.8	35.6	49.5
75 +	36.6	59.2	44.5	55.7

* Rates/100,000.

creased in men from 1970 to 1984, primarily in the age groups 35–44 and 45–54 years (Table III). In the age group 65–74 years the rate remained constant. Among women, incidence rates increased in all age groups 45 years of age and older. Between 1970 and 1984, the total number of reported cases of lung cancer increased from 5,160 to 7,302 among men and from 523 to 956 among women—by 41% and 93%, respectively.

For many years, lung cancer has been the leading cause of deaths due to cancer among men in Czechoslovakia. Lung cancer accounted for 21% of all cancer deaths in 1983.

Age-specific mortality rates for lung cancer have been increasing in most age groups (Table IV). From 1960 to 1983 the age-specific mortality rate among men increased primarily in the age groups 45–54 years and 75 years and older; among women it increased in the age groups 45–54 years and 85 years and older. Among other age groups the age-specific mortality rates increased in both sexes by almost 30–50%, except in the youngest age group.

During the same period, the age-adjusted lung cancer mortality rates (age-adjusted death rates were derived by applying the age-specific death rates to the population distributed by age, as enumerated in 1960) in the Czechoslovak population have been increasing in both sexes, with a slower increase noted among men during the period 1975 to 1983. In the same population, among persons 35 years of age and older, the age-adjusted death rate is consistently increasing in both men and women: in men over 50% and in women almost 50% (Table V). The sex ratio of lung cancer mortality rates has remained nearly constant. In 1960, the age-adjusted death rate was 8.6 times higher among men than women, and in 1983 it was 9.1 times higher among men.

Chronic Bronchitis

According to epidemiologic studies carried out in the last 15 years, cough and phlegm production in the adult population, as symptoms of chronic bronchitis, were found among 25% of male smokers and 4% of male nonsmokers, and in 19% of female smokers and 5% of female nonsmokers.[3,4–6] The frequency of chronic bronchitis in both sexes was related to the amount of cigarettes smoked.[3] The disorder was found in 28% of men and in 20% of women cigarette smokers who had smoked 100,000 cigarettes or more and in 6% of men and 3% of women cigarette smokers who had smoked fewer than 100,000 cigarettes. Among ex-smokers, chronic bronchitis was found in 16% of men and 5% of women. The prevalence of chronic bronchitis in smokers increased among students and apprentices: in 18-year-old men the prevalence of chronic bronchitis was twice as high among smokers as among nonsmokers.

Coronary Heart Disease and Myocardial Infarction

The crude mortality rate for coronary heart disease increased by 13% between 1969 and 1983—from 25.7 to 286.7 per 100,000 inhabitants.[7] The age-adjusted mortality rates for myocardial infarction during the period from 1960 to 1983 increased in both men and women by 37%

TABLE IV. Age-specific Mortality Rates for Lung Cancer by Age and Sex in Czechoslovakia, 1960–1983

Age	1960	1965	1970	1975	1980	1983
Men						
25–34	1.6*	2.3	1.3	1.8	1.7	0.8
35–44	7.0	11.9	15.3	16.1	20.0	17.7
45–54	52.5	60.4	60.7	84.9	116.2	113.6
55–64	230.7	233.0	223.7	252.4	255.1	297.3
65–74	346.0	490.0	522.4	506.2	465.9	466.8
75–84	224.3	356.0	497.8	588.0	612.0	587.4
85 +	69.9	189.8	217.6	320.9	313.2	305.6
Women						
25–34	0.1	0.6	0.5	0.1	0.6	0.5
35–44	2.2	1.5	2.2	2.1	3.7	3.2
45–54	7.1	9.0	7.4	7.8	10.8	13.3
55–64	19.9	18.1	17.7	20.0	21.7	25.8
65–74	31.4	39.9	37.4	34.1	41.4	46.9
75–84	39.8	50.3	54.3	59.9	58.8	57.7
85 +	30.4	73.0	68.5	60.7	58.6	52.7

* Rates/100,000.

TABLE V. Age-adjusted* Mortality Rates for Lung Cancer of the Czechoslovak Population (by Sex and for the Population 35 Years of Age and Older), 1960–1983

	1960	1965	1970	1975	1980	1983
Sex						
Men	54.3†	64.3	67.3	72.3	69.7	75.2
Women	7.0	7.8	7.4	7.2	8.2	9.1
Population ≥ 35 years						
Men	125.7	154.2	163.6	181.4	181.2	196.9
Women	14.7	16.9	16.6	16.8	19.3	21.7

* Age-adjusted to the Czechoslovak population as enumerated in 1960.
† Rates/100,000.

and 39%, respectively (Table VI). A substantial increase can be seen in both sexes during the period from 1965 to 1970. From 1970 to 1983, the age-adjusted mortality rate constantly increased.

Absenteeism Due to Illness

A four-year prospective study examined the influence of the smoking habit on certified absence among wage-earners in a plant.[8] The study revealed a significantly higher absence rate due to sickness in smokers than in nonsmokers: 1.35 times higher than in nonsmokers among men during one year and 1.27 times higher among women ($p < 0.05$). Economic loss resulting from certified absenteeism due to sickness amounted to 10,500 CS crowns (approximately US $1,600) per one smoker of both sexes per year as compared to a nonsmoker.

Legal Measures on Smoking Control

There is no comprehensive law in Czechoslovakia that deals with smoking with respect to its ill effects on health. The Care of People's Health Law of 1966 deals with the state medical care system and public health service. A chapter on healthy living conditions and on the environment discusses tobacco smoking as well as other toxic agents. The details were specified in a decree of the Ministry of Health, "On the Creation and Protection of Healthy Living Conditions." A resolution adopted by the governments of both the Czech and Slovak Socialist Republics and by the Presidium of the Czechoslovak Federal Government on Alcoholism and Other Toxicomanias in 1973 refers to nicotinism as a negative social phenomenon which has to be repressed by governmental, social, and economic measures, and, last but not least, through education.

For nearly ten years cigarette packages manufactured in Czechoslovakia have carried a compulsory warning: "Smoking impairs health."

Apart from these legal provisions dealing with the protection of living and working conditions in general, there are a number of departmental provisions and rules of practice. Consequently, there has been no advertising of tobacco products in the press, over the radio, and on television for more than 40 years. The tobacco industry is state-owned, and imports of cigarettes are kept at a minimum level. The ban on advertising concerns imported cigarettes and tobacco products as well. No sponsorship by the tobacco industry has been allowed in cultural or sports events. Smoking has been prohibited in all passenger trains and buses and on all domestic flights. On international flights, smokers sit separately from nonsmokers. There is a ban on smoking in railway stations and public places such as waiting rooms, cinemas, theaters, and libraries. On express trains, smoking is permitted in special compartments for smokers only. Smoking is prohibited in elementary and secondary schools; teachers may smoke only in separate rooms. At the universities the ban has not yet been fully applied. In health facilities and medical establishments smoking is forbidden for both patients and personnel, except in separate rooms reserved for the purpose. In Slovakia, there is a ban on smoking at all medical staff meetings. Ambulance staffs are not permitted to smoke on duty. Furthermore, medical staffs are required to participate in compulsory antismoking health education.

Smoking is also banned in shops, service rooms, canteens, and in some restaurants, while in other restaurants smoking is forbidden only at mealtime.

There are a number of restrictive measures in other sectors of the national economy which are, however, mainly motivated by concerns about fire. In many organizations and enterprises, participants at public meetings volunteer to abstain from smoking.

There are quite a number of antismoking measures in Czechoslovakia, but they have not yet been combined in a unified legal manner. Until now, all matters concerning smoking control have been jointly handled with anti-alcoholism matters in a central interdepartmental body—the Anti-Alcoholism Council of the Ministry of Health—both in the Czech and Slovak Socialist Republics with branches in all regions and districts of the country. Unfor-

TABLE VI. Age-adjusted* Mortality Rates for Myocardial Infarction for the Czechoslovak Population by Sex, 1960–1983

Sex	1960	1965	1970	1975	1980	1983
Men	59.3†	62.5	134.8	127.2	128.1	161.9
Women	27.3	26.5	58.6	56.8	68.7	69.7

* Age-adjusted to the Czechoslovak population as enumerated in 1960.
† Rates/100,000.

tunately, smoking control has been of only marginal interest for the council. More active in antismoking matters is the Committee on Smoking and Health of the Czechoslovak Pneumological and Phthisiological Society, which mobilizes the support and cooperation of medical personnel.

The most important national activity concerning smoking control is the health education effort of the Health Ministry through its Institute for Health Education. The institute produces a variety of informational materials, including leaflets, manuals, posters, slides, motion pictures, articles and interviews in the newspapers, programs aired on television and radio and over public address systems, and lectures for selected groups. Physicians and medical personnel conduct these compulsory educational programs as part of their ongoing responsibilities. There are compulsory discussions concerning tobacco and smoking in the curricula of the primary and secondary schools. Such a broad spectrum of activity contributes to a positive attitude on the part of the public toward smoking control and creates pressure to enforce further control measures.

The Future

The time has come for the scientific societies of the Czechoslovak Medical Association of J. E. Purkyne to demand the establishment of an advisory body to the Ministry of Health to implement smoking control measures. Members of the body would include physicians, psychologists, sociologists, educators, jurists, and representatives of the mass media, youth organizations, women's organizations, trade unions, and the Red Cross. This advisory body should draft a motion for legislative measures aimed at smoking control. This would then be put before the relevant governmental body for discussion. Smoking control has to be implemented on a broad basis. Activities need to address environmental issues related to cigarette smoking. Health education efforts must be aimed at the prevention of smoking and at its cessation. Social reinforcement must also be present to foster nonsmoking behavior.

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IRRITATING PROPERTIES OF CIGARETTE SMOKE AS INFLUENCED BY HYGROSCOPIC AGENTS

The irritation produced by cigarette smoke should be of great importance to the physician who has under his care the treatment of affections of the nose and throat. Offhand, it is rather difficult to place a definite value upon the importance of cigarette smoke in the production and perpetuation of these throat conditions. For any one patient, however, we may assume that cigarette smoke may play some part in the pathology of the throat condition for which he has consulted his physician.

The source of the tobacco, the flavoring agents, or the paper may each play its part in the qualities of the smoke. But besides these constituents of all cigarettes, there is another which has proved of interest. All cigarettes contain some agent for the maintenance of the proper moisture content of the tobacco. The present study is aimed at the two popular hygroscopic agents, glycerine and diethyleneglycol, and their influence upon the irritant properties of cigarette smoke.

. . . Cigarettes identical in every other respect vary in irritating properties of their smoke, according to the type of hygroscopic agent used. Cigarettes in which glycerine is used are more irritating than when no hygroscopic agent is employed, while those made with diethyleneglycol are definitely less irritating. Our results now show that, regardless of the blend of tobacco, flavoring materials, or method of manufacture, the irritation produced when glycerine is used as the agent is substantially the same—and greater than that caused by diethyleneglycol. . . .

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(*NY State J Med* 1935; 35:590-592)

Smokeless tobacco and concomitant cigarette, pipe, and cigar use among adults in Florida, 1984–1985

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ABSTRACT. One purpose of this epidemiologic field survey of 2,115 adults living in households in Alachua County, Florida, was to determine the prevalence and concurrence of tobacco product use among race, sex, and age groups. Lower rates of cigarette smoking were found than those reported in recent (1980) national surveys, which may reflect a continuing trend of decline in consumption. When all forms of smoking tobacco were considered, no significant differences were found in male/female success rates for quitting. Of all race-sex and age groups, black males 25 years and older were the most likely to use some form of tobacco. Older black females had the highest rates of smokeless tobacco use, and they were rarely smokers. Younger males (18–24 years) reported more smokeless tobacco use than their closest age cohort (25–44 years). Cigarettes are still the "tobacco of choice" for most users; males were much more likely than females to be multiple tobacco product consumers.

(NY State J Med 1986; 86:472–477)

Smoking and other forms of tobacco use began centuries ago in our country's history. After being exported to Europe on Columbus' second voyage in 1493, tobacco gained considerable favor there. Smokeless tobacco was reintroduced into the New World in 1611 by John Rolfe, who grew tobacco in the Jamestown Colony in Virginia. By the 1800s, moist snuff (a pinch of which was held against the gum in the mouth), loose leaf chewing tobacco, and block/plug tobacco enjoyed the most popularity in the United States.[1]

Early in the 1880s, it was observed that spitting facilitated the spread of tuberculosis. At about the same time, the development of machinery enabled the mass production and lower pricing of cigarettes. By 1921, cigarette consumption exceeded other forms of tobacco use for the first time. Smokeless tobacco became mainly a rural phenomenon in the southeast and southwest, especially among workers in textile mills, coal mines, and other industrial sites where smoking was inadvisable.[1]

The aesthetic and sanitary drawbacks of moist snuff and chewing tobacco consumption undoubtedly contributed to their declining popularity. It has been surprising, therefore, to note a recent increase in smokeless tobacco use. The image of a pouch of shredded tobacco or a small, round tin of moist snuff in the hip pocket of a pair of jeans has become increasingly common. In growing numbers, young men have begun to use smokeless tobacco at a time when tobacco consumption in the United States has faltered and gradually declined for a number of years.

The first surgeon general's report[2] linking cigarettes with health risks was followed by increased taxes, threats to price support programs, a coincidental general economic downturn, and the increasingly vocal condemnation of secondhand smoke by "antismoking personalities," as the industry has referred to them.

Social pressure, fear of health consequences from smoking, and price increases may have set the stage for a resurgence of interest in smokeless tobacco, which produces no secondhand smoke, is thought by some users to be a "safe" form of tobacco, and is generally cheaper to use. An upswing in the sale of snuff[3] may be blunted, however, as the health risks of snuff use become more widely known and media advertising is discontinued. The Comprehensive Smokeless Tobacco and Health Education Act (PL 99-252) was signed into law by President Reagan February 27, 1986, and provides for a ban on TV and radio ads by August 27, 1986 and a rotation of three health warnings on packages of smokeless tobacco by February 27, 1987.[4]

The prevalence of snuff use and tobacco chewing is not well known, largely because sales and consumption dropped so low until recently that accurate estimates required prohibitively large study samples of individuals. In 1970, it was estimated that 2.9% of all adult males (those 21 years of age and older) in the United States used snuff; among females, about 1.4% were thought to use snuff. The rates for tobacco chewing were 5.6% for males and 0.6% for females. By 1975, snuff use was estimated to have declined to 2.5% for males and 1.3% for females. Tobacco chewing among males fell to 4.9% while the rate for females remained at 0.6%.[5] During the 1970s, however, the sales of fine cut tobacco used in moist snuff increased 188%; estimates of the number of persons (regardless of age) who use smokeless tobacco in the United States now reach as high as 22 million. As many as 20–40% of adolescent males have tried smokeless tobacco products, and in some areas much higher percentages are being reported.[6]

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Schaefer et al[7] surveyed more than 5,000 junior and senior high school students in schools throughout Texas and reported that 9%, all males, used smokeless tobacco regularly and over half of those started before the age of 13. Eighty-eight percent of the smokeless tobacco users began before the age of 15.

Preliminary findings from the National Institute on Drug Abuse, 1985 National Household Survey on Drug Abuse, suggest that about 16% of males 20 years of age or younger had used smokeless tobacco in the past year while 11% of the males who were 21 or older had consumed smokeless tobacco products. Among females, only 2% of those in either age category reported smokeless tobacco use in the past year. Regionally, the use of snuff and/or chewing tobacco weekly or more often is currently most common in the south (5.0%) and west (4.0%), with lower rates reported in the north central (2.0%) and northeast (1.0%) regions.[8]

Considerably more is known about the use of cigarettes, cigars, and pipes than about smokeless tobacco. For example, in 1955, when smoking was in its heyday, it was estimated that 57.1% of all males 18 and older were cigarette smokers. Only 29.7% of females smoked.[9] In 1980, 36.5% of all males 17 years of age or older were cigarette smokers, compared with 29.1% of females in the same age group.[10]

An optimistic hypothesis would be that persons who are presently under the age of 40 are less likely to be smokers because they had more knowledge of the hazards of smoking while they were growing up. Unfortunately, no such dramatic differences have occurred, but there has been a gradual decline in the rates of smoking in both sexes and in virtually all age groups.[11] Less is known about the prevalence of smokeless tobacco use in conjunction with the smoking of cigarettes, cigars, or pipes. One facet of the present study attempted to measure this phenomenon and to compare rates of adult tobacco use among race, sex, and age groups.

Methods

A multistaged, statistical probability sample stratified for age was utilized in selecting respondents for the study in Alachua County, Florida. A sample of 2,115 persons aged 18 and older were interviewed, with persons 60 years and older oversampled because they were the population of primary interest. Initially, a door-to-door enumeration was conducted in the survey county, producing 231 (10.9%) of the interviews. This method proved to be too slow and labor-intensive. Therefore, random digit dialing techniques developed and tested by the Rand Corporation[12] were initiated and resulted in the completion of 1,733 interviews which comprised 81.9% of the sample. The use of this method systematically included all persons with telephones, even those with unlisted numbers. When a review of the 1980 census of the county indicated that 11.7% of the households did not have telephones and most of these were in predominantly black census tracts, a supplemental enumeration was conducted in those areas. This resulted in 151 interviews or 7.1% of the sample.

Once a household was contacted, enumerators attempted to secure a listing of its members which served as a basis for choosing a specific adult respondent using a procedure developed by Kish.[13] About 7% of the households contacted by telephone would not provide enough information to complete the enumeration. During the second stage of contact, 17.0% of all respondents whose households were enumerated and who were selected for the study refused to be interviewed. An analysis of the age and sex characteristics of the refusals and of the respondents who were successfully interviewed showed remarkable similarities (see Table I).

TABLE I. Age and Sex Composition of Completed Interviews and Refusals

	Completed Interviews (%)	Refusals (%)
Males		
18–24	4.8	5.0
25–44	12.4	13.9
45–64	11.8	11.2
65+	13.3	9.6
Females		
18–24	5.7	5.7
25–44	14.2	12.8
45–64	14.9	19.6
65+	22.8	22.3

An additional 12.2% of the enumerated households resulted in noncompletions. Most (7.3%) of these were a result of respondents' moving from this highly transient area, or being unreachable after numerous attempts to contact them. The remainder were too ill or otherwise unable to be interviewed.

Respondents were sent a letter which outlined the study and enlisted their assistance. This letter was followed by a telephone call during which an attempt was made to schedule an interview. All interviews, which lasted an average of 1.5 hours, were conducted face-to-face, usually in the respondent's home.

The interview schedule was a comprehensive and integrated one which included 280 major items, many of which had a large number of nested subsets. Twenty items established current and former tobacco use, including that of smokeless tobacco, cigarettes, cigars, and pipes. The instrument contained the standard social and demographic questions about age, sex, race, socioeconomic status, and marital histories.

The sociodemographic characteristics of the sample are displayed in Table II. The sample is shown unweighted even though it represents a deliberate oversampling of persons 60 years of age and older. Alachua County contains the University of Florida in Gainesville which has an enrollment of approximately 36,000 students. Therefore, weighting the sample to fit county characteristics for age, sex, and race tends to skew the distribution in

TABLE II. Characteristics of the Sample (N = 2,115)

	N	%
Sex		
Males	897	42.4
Females	1,218	57.6
Race		
White	1,648	77.9
Black	450	21.3
Other	17	0.8
Race-sex		
White Males	743	35.4
White Females	905	43.1
Black Males	144	6.9
Black Females	306	14.6
Age		
18–24	223	10.5
25–34	346	16.4
35–44	217	10.3
45–54	177	8.4
55–64	386	18.3
65–74	488	23.1
75+	277	13.1

TABLE III. Population Comparisons by Race, Sex, and Age: Alachua County, Florida, 1984, and Alachua County Survey Sample, 1984–1985*

	1984 Alachua County Estimates		1984–1985 Survey Sample			1984 Alachua County Estimates		1984–1985 Survey Sample	
	N	%	N	%		N	%	N	%
White					**Black**				
Males†	55,939	43.1	752	35.6	**Males**	9,206	7.1	144	6.8
18–24	19,389	15.0	89	4.2	18–24	2,332	1.8	13	0.6
25–34	15,425	11.9	148	7.0	25–34	2,464	1.9	16	0.8
35–44	8,125	6.3	79	3.7	35–44	1,444	1.1	20	0.9
45–54	5,010	3.9	59	2.8	45–54	1,020	0.8	16	0.8
55–64	3,973	3.1	153	7.2	55–64	819	0.6	21	1.0
65–74	2,661	2.1	154	7.3	65–74	714	0.6	38	1.8
75+	1,356	1.0	70	3.3	75+	413	0.3	20	0.9
White					**Black**				
Females†	52,921	40.8	912	43.1	**Females**	11,583	8.9	306	14.5
18–24	16,871	13.0	89	4.2	18–24	2,871	2.2	32	1.5
25–34	12,923	10.0	131	6.2	25–34	2,924	2.3	51	2.4
35–44	7,855	6.1	91	4.3	35–44	1,876	1.4	27	1.3
45–54	5,140	4.0	81	3.8	45–54	1,243	1.0	21	1.0
55–64	4,381	3.4	158	7.5	55–64	1,054	0.8	54	2.6
65–74	3,373	2.6	220	10.4	65–74	944	0.7	76	3.6
75+	2,378	1.8	142	6.7	75+	671	0.5	45	2.1

* Percentages are based on the Alachua County population estimate of 129,649 persons 18 years of age and older, and on the survey sample total of 2,114 respondents.
† In this case, "white" actually refers to "nonblack" because county estimates were available in that designation only.

the opposite direction with a "younger" sample being the result. Since we noted an unusually high rate of smokeless tobacco use among older black females, the original sample characteristics were retained for purposes of this paper so that cell sizes for those age groups would facilitate analyses (Table III).

Results

Our findings on smoking and smokeless tobacco consumption in Alachua County are presented in juxtaposition with national norms in Table IV. Although every survey of tobacco use has some variations in sample selection, question wording, and administration, it is possible to detect time trends and patterns by comparing similar items. For example, a common question asked in surveys of smoking behavior is whether or not the respondent smokes cigarettes. Thirty years of cigarette smoking patterns in the U.S. are shown in Table IV. Since differences can occur between self-report and proxy-reported tobacco consumption, this table was specifically limited to the former source of information.

There are slight variations in ages represented, but the gradual decline in levels of smoking is clear. Among males, in virtually every age group there is a decrease in the percentages of current smokers with each succeeding time frame. It is important to remember, of course, that these are cross-sectional survey findings, therefore different individuals were interviewed each time. Also, there is no way to clearly understand the extent to which mortality from cigarette smoking would alter the characteristics of the older age groups.

Even less clear is the pattern for females. Keeping in mind that the first surgeon general's report on smoking and health was issued in 1964, it is interesting to note an *increase* in smoking among all age groups of females between 1955 and 1966 while males experienced a decrease in cigarette smoking. By 1970, a small decline occurred among younger females, but the rates of smoking among women aged 45 and older continued to rise.

In our present study, reported in Table IV in the column headed "1984–1985," some variations may be seen in the percentages of smokers in each age group. In general, we found lower rates of cigarette smoking than are shown in the most recent (1980) US survey. These differences may be the result of a continuing and accelerated decline in smoking during the five years which elapsed, they may reflect regional differences, and/or they may represent racial variations in the samples.

The statistics for current smokers shown in Table IV might lead one to infer that women have quit smoking in lower proportions than have men, and, further, that this means they find it harder to quit. This conclusion was stated in a surgeon general's report which focused on women and smoking.[14] This is challenged by Jarvis,[15] who concludes that when he adjusted for the switch to cigars by men who quit smoking cigarettes, the sex differences in cessation are virtually eliminated.

Not shown in Table IV is our comparison of current and former smokers of any tobacco products among males and females in the same four age groups. The analysis looked only at "ever" smokers. With no regard for type of tobacco smoked, any significant male/

TABLE IV. Self-reported Cigarette Smoking, United States, 1955–1980 and Alachua County, Florida, 1984–1985

	Percentage of Persons Who Are Current Cigarette Smokers				
	1955*	1966*	1970†	1980†	1984–1985‡
Total	39.9	40.2	36.7	32.6	§
Males	57.1	49.9	43.2	36.5	§
18–24	63.2	56.3	40.6	32.0	25.7
25–44	67.9	60.8	50.6	42.5	28.5
45–64	56.6	52.5	44.6	40.3	31.5
65+	27.5	26.1	23.0	17.8	22.3
Females	29.7	33.5	30.9	29.1	§
18–24	38.7	40.4	30.2	30.7	24.8
25–44	39.8	42.9	38.6	32.8	23.4
45–64	21.7	31.2	32.8	30.5	26.9
65+	5.3	8.2	10.9	16.7	12.4

* US Public Health Service, Vital and Health Statistics, Series 10, No. 59, p 20, 1970.
† US Bureau of the Census, Statistical Abstract of the United States: 1985, p 119 (based on persons 17 years old and over).
‡ Alachua County sample, N = 2,112, 1984–1985.
§ The atypical age distribution of the Alachua County sample makes comparisons inappropriate for these categories.

female differences in proportions of smokers disappeared completely. This finding tends to support Jarvis' contention that males and females have the same proportions of "quitters" if one includes all forms of smoking material.

Comparisons of smoking behavior among race-sex and age groups reveal some interesting variations associated with race.

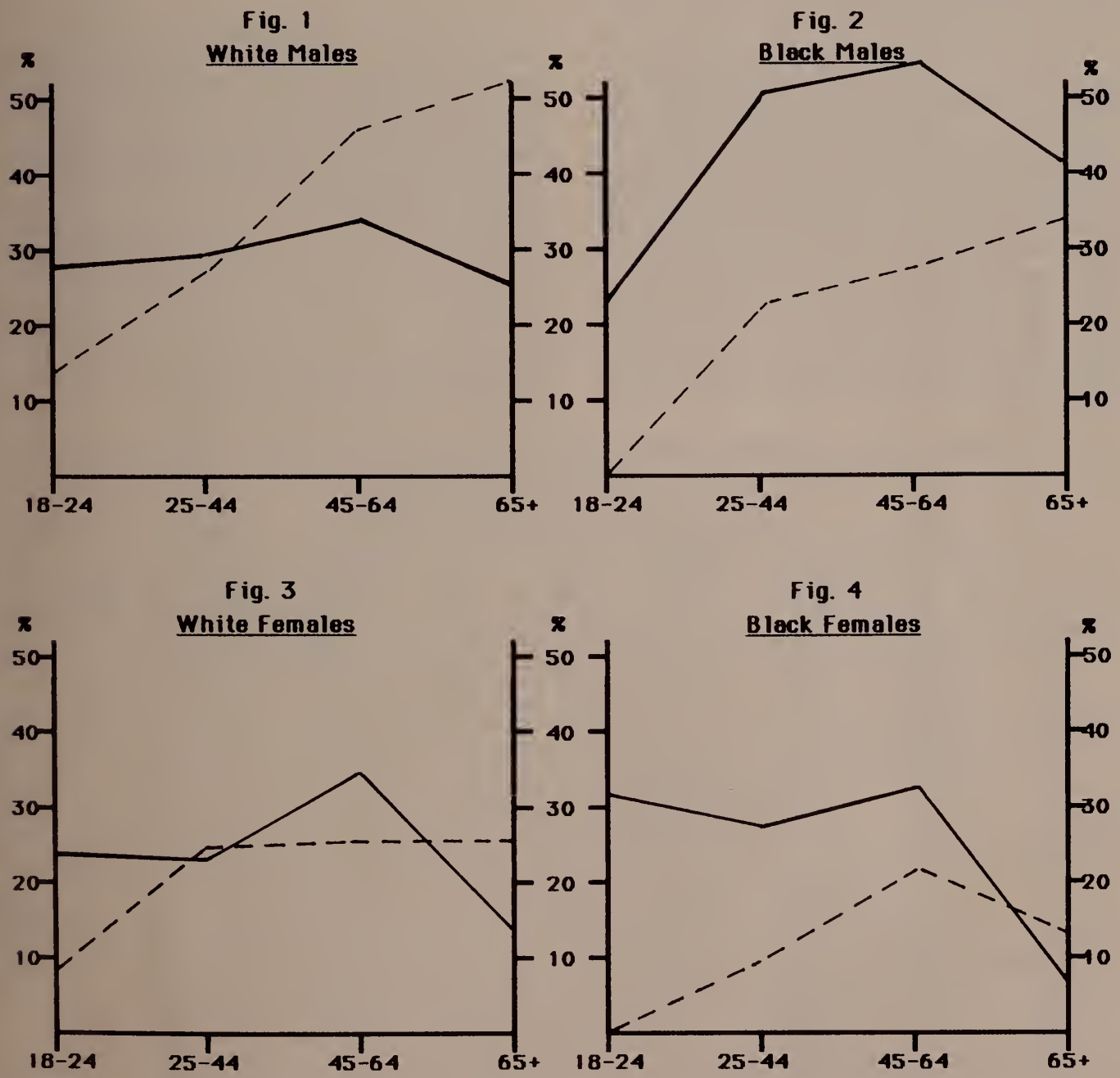
Figures 1–4 illustrate the extent to which current and former smokers are found among race-sex groups of various ages. Not surprisingly, there are more current smokers than former smokers among all race-sex groups within the ages of 18–24. This is also true among those aged 25–44, but the proportion of former smokers among whites in that age group is almost the same as the percentage of current smokers. Also among whites, the proportion of former smokers exceeds that of current smokers in the 45 years and older age groups. This is not true of blacks, although there tends to be a convergence of the percentages of current and former smokers among persons aged 65 and older.

Among black females aged 18–24, 31.3% were smokers. This rate exceeds that of all other race-sex groups in that age category. Half of all black males aged 25–44 reported being smokers, 54% of those aged 45–64 smoked, and 41 percent of black males 65 and older admitted smoking. Therefore, among race-sex/age groups, blacks (especially males) were more likely than whites to be smokers.

Although all race-sex groups reported more former smokers among the older age groups, white males aged 65 and older were particularly likely to have quit smoking (51.6%).

Figure 5 presents rates of smokeless tobacco use in the sample among race-sex and age groups. In this analysis, no control is made for other tobacco use, therefore respondents who are shown as smokeless tobacco users may also be smokers.

In general, black males were more likely to use smokeless tobacco than were white males. This was especially true of the youngest (18–24 years) and oldest (65+ years) age groups. Black females 65 and older had the highest rates of smokeless tobacco use (23.1%) of any



FIGURES 1–4. Percent of race-sex/age group who are current smokers (solid line) or former smokers (broken line) (N = 2,086).

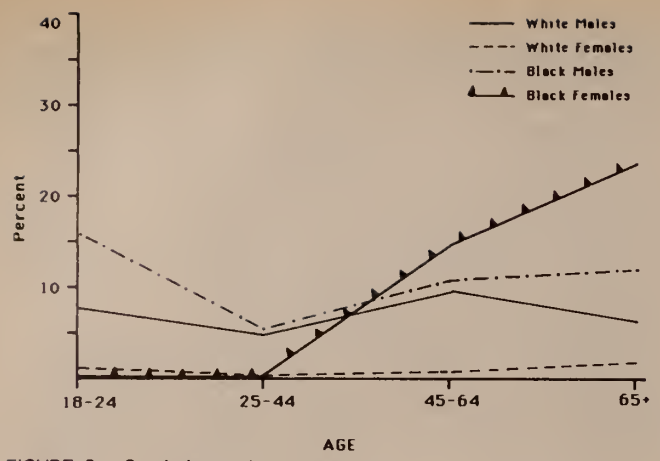


FIGURE 5. Smokeless tobacco use by race, sex, and age, Alachua County, Florida, 1984–1985 (N = 2,095).

race-sex/age group. Both white and black males aged 18–24 reported higher rates of chewing and dipping than their 25–44-year-old age cohorts. This may signal an upsurge in use among young males, as has been suggested recently.[8]

A summary of tobacco product use of any kind is presented in Table V. Black males, especially those over 25 years of age, were more likely than any other race-sex group to use some form of tobacco. White females, in general, and those aged 65 and older, in particular, were least likely to be either smokers or chewers/dippers. The heaviest use of cigarettes to the exclusion of other forms of tobacco was found among black males aged 25–44. The smoking of cigars only was most common among black males aged 65 and older. Pipe smoking (with no other tobacco used concurrently) occurred only among white males. Black females aged 45 years and older were most likely to use only smokeless tobacco; they were rarely smokers as well as chewers and/or dippers. On the other hand, black males reported the highest concurrent use of smokeless and smoking tobacco. This was most common among men 18–24 years of age.

We might conclude from Table V that black males represent a particularly high risk group for tobacco related health problems. Nonetheless, it is white males who represent the largest number of potential candidates for problems from tobacco use, despite their somewhat lower rates of consumption compared with black males. Using 1984 estimates of the US population, we would expect 25.5 million white males 18 years of age or older to be tobacco users while only 4 million black males would be "at risk." Among females, we would estimate that 17.5 million white females and 3.3 million black females of that age group smoke and/or dip/chew tobacco at present. Altogether, approximately 50 million Americans 18 years of age or older use some form of tobacco. Furthermore, that figure does not reflect the full magnitude of the behavior since it does not include younger users. This large group represents a unique challenge to health educators and public health officials.

Discussion

In this survey of tobacco use among adults in Alachua County, Florida (1984–1985), we found somewhat lower rates of cigarette smoking than were reported in recent (1980) national surveys in the United States. These differences may represent a continuation of the general decline in consumption which is occurring nationwide or they may reflect regional variations.

Although some studies have suggested that women find it more difficult than men to quit smoking cigarettes, we found only marginal differences in some age groups and none at all in others. When we included all forms of smoking tobacco in the analysis, we found even stronger support for the theory that male/female quitting successes are virtually identical when one does not exclude cigars and pipes from consideration.

TABLE V. Concomitant Use of Tobacco Products by Race-Sex and Age Groups (N = 2,095)

		Tobacco Use* (% of Race-Sex-Age Group)						
		No Tobacco	Cigarettes Only	Cigars Only	Pipes Only	Smokeless Only	Smoking and Smokeless	Other Smoking
White Males	741							
18–24	83	66.3	20.5	1.2	0.0	6.0	1.2	4.8
25–44	224	68.8	19.2	0.4	2.2	2.2	2.7	4.5
45–64	211	60.2	21.3	0.9	1.9	6.2	2.8	6.6
65+	223	69.5	15.2	2.7	2.7	4.0	2.2	3.6
White Females	904							
18–24	87	75.9	23.0			1.1	0.0	
25–44	219	77.6	22.4			0.0	0.0	
45–64	238	73.5	25.6			0.8	0.0	
65+	360	84.7	13.6			1.4	0.3	
Black Males	144							
18–24	13	76.9	7.7	0.0		0.0	15.4	0.0
25–44	36	44.4	44.4	2.8		5.6	0.0	2.8
45–64	37	43.2	29.7	2.7		2.7	8.1	13.5
65+	58	51.7	27.6	5.2		6.9	5.2	3.4
Black Females	306							
18–24	32	68.8	31.3			0.0	0.0	
25–44	78	73.1	26.9			0.0	0.0	
45–64	75	56.0	29.3			12.0	2.7	
65+	121	70.2	6.6			22.3	0.8	

* Mutually exclusive categories

A comparison of current and former smokers by race-sex and age revealed that while there are more current smokers among the young age groups, the proportion of former smokers tends to increase with age. By age 65, the percentage of former smokers exceeds that of current smokers in every race-sex category except that of black males.

Among race-sex groups 18–24 years of age, the highest proportion of smoking was reported by black females. In the other age groups, black males were overrepresented, with almost half being smokers.

Black females 65 years of age and older had the highest rates of smokeless tobacco use of any race-sex age group; they were rarely smokers as well as chewers and/or dippers. Younger males (18–24 years) of both races reported higher rates of use than their next older cohorts, those aged 25–44.

Black males, especially those aged 25 or older, were the most likely of all race-sex age groups to use some form of tobacco. White females were least likely to smoke, chew, or dip.

Pipe smoking to the exclusion of all other tobacco products was reported by no one other than white males. Cigarettes were clearly the "tobacco of choice" for most users, especially black males 25–44 years of age. Males were much more likely than females to be multiple tobacco product consumers.

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FROM THE LIBRARY

CIGARETTE SMOKE AS A HEALTH HAZARD

It has been said frequently, and with some justification, that the medical profession broke faith with the public in failing to inveigh vigorously against smoking as a menace to health. But it can never be held against our profession that it permitted itself, even by implication, to be involved in the endorsement of a tobacco product.

The cigarette industry is not a commodity business; by this I mean that the individual manufacturer makes no honest, wholehearted effort to claim a commodity better than his competitors. Each makes a cigarette that he feels will satisfy the public taste; he proceeds to exploit it by a type of advertising that concerns itself not at all with the inherent qualities of the commodity. In its truest sense the manufacturer's real commodity must never be discussed; it is taboo. A little reflection reveals the real commodity to be smoke—the dry, destructive distillation of wood (leaves); and what this smoke contains must be sung *sotto voce*. And so, carbon monoxide, ammonia, prussic acid, acetic acid, aldehydes including acrolein, the alkaloid nicotine and pyrrol, pyridine and other heterocyclic nitrogenous bases (generically grouped under the term "tars"), all products of the distillation and contained in the smoke, had best be forgotten for the greater happiness, perhaps, of the consuming public.

. . . The tobacco industry, like all others, concerns itself with making money. It is an industry centuries old, steeped in an art that defies the amateurish dabblings of intruders and hypnotized into a belief in the sacredness of the leaves that are cured and blended. This latter spirit it has successfully striven to instill in the consuming public, with the result that there has been achieved for the industry a false public psychology, from which the industry, unmolested, or if you will, unassisted, will never dare retreat. The belief that cigarettes contain only pure, unadulterated tobacco is almost universal among smokers, and while vaguely aware of flavorings in tobacco mixtures, they are blissfully ignorant of the ungodly messes of which they are composed. Having once taken the position that smoke quality is merely a matter of the quality and purity of tobacco, there is no place for publicity on the adulterants used in making the cigarette as good and as acceptable as it is . . .

HERMAN SHARLIT, MD
(*NY State J Med* 1935; 35:1159–1161)

Cigarette prices and cigarette consumption in Austria, 1955–1983

GABRIELE F. WÖRGÖTTER, PHD, MICHAEL KUNZE, MD

Smoking control is possible through a variety of means, including smoking cessation, health education, and legislation. All of these approaches require careful planning and continuous evaluation. Austria has been dealing with its tobacco problem for a number of years, and some positive developments have resulted, including effects on price policy and taxation.

BACKGROUND INFORMATION

To evaluate past antismoking activities in Austria and to design future actions aimed at reducing cigarette consumption, it is important to understand the main determinants of the volume of tobacco consumption. This paper examines these factors and discusses tobacco product prices relative to those of other consumer goods, as well as the effect of price policy on cigarette consumption between 1955 and 1983. We also present a model of tobacco consumption and parameter estimations for this model.

The data in Table I demonstrate the importance of relative prices and total consumption of consumer goods on the volume of tobacco consumed. During the period 1972–1983, relative prices remained constant, whereas from 1955 to 1972, tobacco product prices rose by 1.4% less than prices of nontobacco consumer goods. Additionally, increases in total consumption of goods fell from 4.8% to 3.0%. During the same time, the average increase of tobacco consumption fell from 5.4% to 1.8%.

THE MODEL

In order to estimate the influence of relative prices, total consumption trend components, and measures taken by the Austrian Ministry of Health and Environment Protection on tobacco consumption, the following log-linear relationship was established:

$$\Delta tc_t = a + b\Delta rp_t + c\Delta tpc_t + dD_{74} + et$$

The variables tc, rp, and tpc denote the logarithms of tobacco consumption (at constant prices of 1964), relative prices, and total private consumption, respectively. The symbol Δ refers to the change of this variable compared with the previous year. The subscript t indicates the time period. The term D_{74} is a dummy variable, which is equal to one in 1974 and zero otherwise. (In 1974, systematic "stop smoking" efforts were instituted by the public health administration in Austria.) The last term, et, refers to a systematic and autonomous change in the growth rates of tobacco consumption.* The advantage of the log-linear form of this model lies in the possible interpretation of the parameters (especially b and c) as elasticities.†

TABLE I. Tobacco Consumption, Relative Prices Between Tobacco and Other Consumer Goods, and Total Private Consumption, Austria, 1955–1983

Time Period	Average relative changes from year to year: Tobacco Consumption	Relative Prices	Total Consumption
1955–1972	+5.4%	−1.4%	+4.8%
1972–1983	+1.8%	−0.04%	+3.0%
1955–1983	+4.0%	−1.0%	+4.1%

ESTIMATED RESULTS

The unknown parameters of the model have been estimated by the method of ordinary least squares using yearly Austrian data from 1961 to 1983. The reason for the reduction of the observation period lies in the development of tobacco and total private consumption in the years 1955 to 1960, which would introduce a bias into the estimation results.‡ The following results were obtained:

$$\Delta tc_t = \underset{(0.020)}{0.067} - \underset{(0.121)}{0.540}\Delta rp_t + \underset{(0.0251)}{0.358}\Delta tpc_t - \underset{(0.0222)}{0.0613}D_{74} - \underset{(0.00072)}{0.00246}t$$

The numbers in parentheses are the estimated standard deviations of the estimated coefficients. R^2 (0.756) is the

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* The variable t represents a linear trend (equal to one in 1954 and 30 in 1983). The coefficient e measures by how much the autonomous growth rate of tobacco consumption changes from year to year.

† The parameters b and c reveal by how many percentage points tobacco consumption changes if relative tobacco prices (total consumption) change by 1% respectively.

‡ By inspection of the residuals from the regression using all observations from 1955 to 1983, it was apparent that tobacco consumption had been systematically overestimated from 1955 to 1969. Upon testing whether the observations from 1955 to 1960 belonged to the same sample as the other observations, we had to reject the hypothesis at the 95% significance level.

coefficient of determination; SD (0.0197) is the standard deviation of the estimated residuals; and DW (1.053) is the Durbin-Watson test for first order autocorrelation.

The general characteristics of the estimation results are satisfactory. All estimated parameters have the expected signs and sizes. All parameters, except c, are significantly different from zero (at the 95% confidence level). The estimated R^2 value indicates that approximately three quarters of the variation in the level of tobacco consumption can be "explained" by this model.[§] The standard deviation of the unexplained changes in tobacco consumption growth is approximately 2%. The Durbin-Watson test does not indicate any first order autocorrelation.

These data indicate the following:

- Austrian tobacco consumption is price-inelastic. A 1% increase in relative tobacco prices decreases tobacco consumption by only 0.540%. This means that an increase in taxes on tobacco products would not reduce tax revenues by much. This would occur only if the relative price elasticity exceeded 1%.
- Tobacco consumption is relatively independent of general consumption patterns. Coefficient c takes the value 0.358 in our estimation, but is not significantly different from zero.
- The autonomous component of tobacco consumption growth has been very strong in the past (nearly 7% in 1961), but is estimated to decline by 0.25% per year. Its estimated value for 1983 is 1%.
- The efforts of the public health service to reduce cigarette smoking since 1974 are estimated to have had a permanent effect of more than 6%.

[§] This should not be interpreted as proof of causality. All we can (and want to) say is that the Austrian data we examined do not contradict the simple model of tobacco consumption presented in this paper.

Conclusions

These analyses show that smoking control measures have been successful in Austria. But there is great potential for additional progress if more sophisticated price policies are implemented. Tobacco consumption in Austria could be stabilized by instituting price increases of 1.3% annually, if one assumes that total private consumption increases by 2% per year. Any autonomous increase of tobacco consumption by 1% would make it necessary to increase relative tobacco prices by almost 2% in order to keep total tobacco consumption constant.

From the public health point of view, the only desirable goal of various interventions is a decrease in cigarette consumption. Even modest but continuous price increases would be very helpful in achieving this objective. It is obvious that Austria has not been using price policy in a way that would help both conflicting interests, health policy and fiscal revenues. It is possible to simultaneously decrease cigarette consumption and increase tax revenues. At present, price policy and taxation are among the most powerful tools available to control the smoking epidemic.

GOVERNMENT INVOLVEMENT IN SMOKING AND HEALTH

The Office on Smoking and Health is the focal point for all smoke-related activities of the Department of Health and Human Services.

The Office prepares and disseminates the annual Surgeon General's reports on smoking, the last several of which have honed in on specific aspects of the problem: *The Health Consequences of Smoking, The Behavioral Aspects of Smoking, Education, and Prevention* (1979); *The Health Consequences of Smoking for Women* (1980); *The Changing Cigarette* (1981); *Cancer* (1982); and *Cardiovascular Disease* (1983).

Using computer and microfilm, the Office's Technical Information Center serves researchers by providing literature searches, references, abstracts, and copies of articles.

In addition, the Center publishes the periodic *Smoking and Health Bulletin*, an annual cumulation of abstracts of research papers (*Bibliography on Smoking and Health*), the biennial *Directory of Ongoing Research in Smoking and Health*, and an annual summary of legislative actions (*State Legislation on Smoking and Health*).

The Office is responsible for analyzing scientific information for the purpose of maintaining federal smoking policies. It is one of four centers serving the bibliographic needs of the World Health Organization on smoking and health.

The Office develops educational programs and public service announcements targeted to women, ethnic minorities, teens, and children, and disseminates model programs both for preventing teenage smoking and for encouraging smoking cessation.

To be placed on the Office mailing list or to receive further information about its services, write to:

Department of Health and Human Services
Office on Smoking and Health
Technical Information Center

5600 Fishers Lane
Park Bldg., Rm. 1-10
Rockville, MD 20857

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Antismoking publicity in Scotland: A decade of progress

GERARD B. HASTINGS, BSc, DOUGLAS S. LEATHAR, PhD

INTRODUCTION

The Scottish Health Education Group (SHEG) is the government body responsible for health education in Scotland. Its work covers all the major health education topics, from antenatal care to gerontology. In addressing these issues it has become involved in approaches as diverse as self-help groups, political lobbying, and mass media advertising. This paper discusses SHEG's use of mass media antismoking advertising.

SHEG's use of the mass media is of interest because it is grounded in advertising research. Consumer input has guided the conception, development, and evaluation of campaigns, and this process has been applied in a continuous, sequential, and cyclical manner. This approach is not unusual among commercial advertisers but is still a rarity in health education, at least in Europe. Most of SHEG's research has been conducted by the Advertising Research Unit (ARU) at Strathclyde University, which was established in 1979 under the auspices of SHEG for this specific purpose. The combination of consistent research and researchers has contributed to particularly innovative and creative campaigns. SHEG's work in the area of antismoking provides a good illustration of this.

The campaigns discussed below were developed over a period of about seven years, during which time SHEG's approach evolved from a problem-specific, negative one, designed to discourage specific "undesirable" behaviors, to a positive, "whole-person" approach that emphasizes the physical, psychological, and social benefits of prohealth decision making.

Four stages can be distinguished in this process of change:

1. Increasing uncertainty and ultimate disenchantment with the conventional approach, where the emphasis was on the promotion of negative messages about the risks of smoking.
2. Attempts to produce material that promoted positive messages about nonsmoking rather than negative ones about smoking—the development of the so-called "positive nonsmoking concept."
3. The realization of a need for a broader change in SHEG's media policy—the birth of the "Be All You Can Be" positive health "umbrella" campaign.
4. Renewed attempts to produce a positive nonsmoking campaign.

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NEGATIVE MESSAGE PROMOTION

Toward the end of the 1970s, SHEG was becoming increasingly uncertain about the value of antismoking campaigns that limited themselves to the promotion of negative and usually hardhitting messages about smoking. There was mounting evidence that the majority of the Scottish population was aware of the health risks of smoking (P. P. Aitken and D. S. Leathar, unpublished data, 1981), and, indeed, that nearly two thirds of smokers had at some time tried to give up the habit.[1] Given these circumstances, the continual repetition of messages about these risks appeared unnecessary. Indeed, it was argued, such repetition could even be counterproductive because it would generate anxiety, which, if it could not be resolved behaviorally (through giving up smoking), would be resolved psychologically, through ignoring or misinterpreting messages, or rationalizing the risks they emphasized.

SHEG's uncertainty was increased when pretesting confirmed that negative material did cause anxiety which led to defensiveness. Interviews revealed that the negative material evoked, among other reactions, anger, aggression, guilt, embarrassment, and general distress, which was expressed both verbally and nonverbally. Aggression, for example, might be expressed by the use of colorful language or, as in one instance, by the destruction of tape recorders by interview subjects who had been drinking heavily.

A defensive response to content showed itself in apparently idiosyncratic ways. A classic example of this occurred in connection with the poster depicted in Figure 1. This poster was developed to publicize the government health warning (GHW) which in the United Kingdom is printed on every cigarette packet and at the bottom of every press and poster cigarette advertisement. Well received within the advertising world, the poster was praised as an elegant symbolic representation of the link between smoking and ill-health, with the bottom copy line linking the symbolic material to the GHW itself.

WHY DO YOU THINK
EVERY PACKET CARRIES A GOVERNMENT HEALTH WARNING?

FIGURE 1. Poster developed to publicize the government health warning against smoking.

When the original version of this advertisement was pretested,[2] however, only nonsmokers perceived it accurately. Smokers, on the other hand, showed a marked perceptual defensiveness toward the entire ad, particularly to the bottom copy line, "Why do you think every packet carries a government health warning?" This they perceived as the actual government warning itself, which, because they disliked what it said, they claimed not to see. Thus, smokers saw the ad as strictly pictorial material without its copy line. Viewed in this context, the advertisement was subject to a variety of misinterpretations. The symbolic tombstone, for example, was seen by some smokers as a pillar of rock, a lipstick, or a telegraph pole, while the background image was perceived as a pleasant, idyllic field rather than as a threatening graveyard.

The final advertisement was reconstructed to enable smokers to perceive it the same way nonsmokers did. Since misperception of the bottom copy line was due to smokers' perceptual defensiveness rather than to any intrinsic fault in the ad's technical clarity, the line "Ashes to ashes" was introduced to further link the copy to the visual material. Technically, there was then an excess of information on the same basic death theme (the "Ashes to ashes" line, "RIP," the wreath, the black garland, the tombstone, and the graveyard). Despite this, the concept itself was apparently so threatening that although the smokers' initial misperceptions were avoided in the new version, the revised ad induced yet another defensive reaction: Smokers simply rationalized and dismissed the message. Respondents argued that death could occur at any time, irrespective of smoking ("You could walk in front of a bus tomorrow"), or that the health hazards of smoking were overstated ("My granny lived till she was 102 and she smoked all her life").

This advertisement illustrated two defensive phenomena that can be encountered in health education publicity. First, the threatening nature of the campaign can lead to its being psychologically misperceived. Second, the message is likely to be rationalized and thus dismissed if the campaign merely induces anxiety without providing an appropriate means of resolving it.

Positive Nonsmoking

The problems of defensiveness led SHEG to reconsider its antismoking strategy, and to replace the traditionally negative antismoking message with a positive nonsmoking message that concentrated on the positive benefits of not smoking rather than on the negative aspects of smoking. The first attempt to do this was targeted at young people (10–14-year-olds) who had not yet taken up smoking but who were increasingly exposed to tobacco.

The material SHEG commissioned consisted of four animated test films, each promoting a mythical antismoking product:

- "Kof," a sweet that gave the eater a sore throat, a fuzzy head, smelly breath, and ulcers
- "Ashtré," a hairspray that gave the user smelly hair
- "Nicotene," a toothpaste that gave the user smelly breath and stained teeth
- "Stub," an aftershave that made the user smell of stale cigarettes

The ARU pretested this material with 10–14-year-olds (D. S. Leathar and G. B. Hastings, unpublished data, 1980) and with 16–24-year-olds (both smokers and nonsmokers). The research showed that the sophisticated style of the films and the subtle use of sarcastic humor to communicate the message resulted in confusion and misinterpretation for many of the younger respondents (those 14 years of age and younger). This confusion was most clearly and frequently expressed in the belief that the films were promoting real products that would appear on the market and could actually be purchased.

The vast majority of older respondents understood the films as promoting an antismoking message. However, the message was seen to be exactly that—antismoking. The films underlined the dangers and drawbacks of smoking and did not promote a positive attitude to nonsmoking. Respondents reacted to the threatening messages by rationalizing the dangers. Thus, respondents indicated that cigarettes did not cause bad but smoky breath, stained teeth could be cleaned with special toothpaste, smelly hair could result as much from sitting in a smoky atmosphere as from smoking, and you might even date a girl who likes you to smell of smoke!

The films did not fulfill either of their two basic requirements: They did not communicate successfully with 10–14-year-olds, nor did they promote a positive nonsmoking message.

SHEG's next attempt at a positive nonsmoking commercial also ran into problems. The commercial was again aimed at 10–14-year-olds. Rough concept material was

produced based on the slogan "No Smokers Breathe Easy," which was presented in the form of a lively and light-hearted jingle. The material was tested qualitatively, in group discussions with the target audience (G. B. Hastings, unpublished data, 1981). The initial response was confused and uncertain. Respondents could not understand how material that addressed a topic as serious as smoking, which they strongly associated with threatening consequences such as cancer, could be so light-hearted and happy. Furthermore, the style of the material clashed with their expectations of what health education in general, and especially health education on this topic, should be like. In their experience, antismoking material was always solemn and portentous.

As a result of this conflict between their expectations and the material, the respondents' immediate inclination was to reject it as inappropriate. Only after detailed discussion in the groups did some see it in a different light, and distinguish it from antismoking material they had seen in the past. As one respondent expressed it: "The others [traditional antismoking material] are telling you what smoking does to you. This one is telling you what *not* smoking does—how it helps you."

In other words, the material gradually came to be seen as providing a positive nonsmoking message. This change in understanding of the material led to a change in attitude towards it. The material then seemed appropriate to the message and was more appealing to respondents.

These findings suggested that while the material had considerable potential, it would be difficult to realize because of the need to overcome consumer perceptions that predefined antismoking material as negative and solemn. Overcoming these expectations in the research group had required an hour of detailed discussion. In the real world, this would be much more difficult to achieve. Thus, it seemed that at best the material might have long term potential, but was of doubtful value in the short term. In broader terms, SHEG's whole antismoking strategy had encountered a Catch 22 situation. On the one hand, there was a clear need to move away from a purely negative approach in this area, but on the other, consumer perceptions were such that any move in this direction was likely to be judged as inappropriate. The only way forward seemed to be for SHEG to try to change consumer expectations about antismoking publicity.

In considering this possibility, SHEG considered the example set by the tobacco companies. These organizations promote products that are antisocial, unhygienic, expensive, injurious to health, and potentially deadly. Yet they advertise these items using campaigns that are steeped in positive imagery.[3] If this could be done with a product as intrinsically negative as tobacco, surely SHEG could achieve similar success when, in broad terms, it was promoting an intrinsically positive product—good health. Perhaps predictably, it was this broader approach that provided SHEG with the means to make further progress with its antismoking material.

Positive Health

Because of SHEG's association with the ARU, its mass media material on a wide range of topics has been consistently researched. The research has covered basic problem definition, developmental research, and postcampaign evaluation. The resulting data have made it possible to isolate a number of recurrent problems in SHEG's mass media work. In addition to the previously discussed problems of negative material, these included its often being seen as:

- *Middle class rather than working class oriented*, in both content and style.
- *Authoritarian rather than empathetic.* The material seemed to be telling people what to do and how to run their lives, rather than enabling and encouraging them to make their own informed health decisions.
- *Promoting long term rather than short term messages.* For example, antismoking material emphasized the health risks of cigarettes, many of which are very long term and probabilistic.
- *Fragmented.* Campaigns tended not to have integrated, strategic objectives, operating in isolation rather than providing the focus for an interactive strategy involving other health professionals, parents, teachers, etc.
- *Topic based rather than whole-person oriented.* For example, separate campaigns were run on drinking, smoking, and contraception. This ignored the fact that these activities can overlap and often reflect the individual's overall life-style rather than isolated problems within it.

In some instances these weaknesses were overcome during pretesting of individual campaigns. SHEG's alcohol material was carefully designed to depict ordinary working class drinking (showing appropriate bars, social settings, language, etc). It also attempted to avoid being didactic and overemphasizing long term messages.

This individual campaign approach was not always successful, however. Attempts to make antismoking publicity more positive had largely failed. Furthermore, other weaknesses, such as fragmented strategic approaches and the advertising's tendency to be topic based, could never be overcome within individual campaigns. These problems suggested a need for an overview or "umbrella" campaign to pull together and promote the basic themes underlying modern health education—in short, a campaign promoting good health in much the same way as a marketing company would promote its corporate identity.

This campaign had several key requirements. First, and most important, the concept presented had to emphasize the advantages of healthy life-styles, such as enhancing self-esteem, self-fulfillment, and mental well-being. Second, although the overall umbrella concept was intended to promote common themes, it also had to be capable of being applied to specific health topics as and when required. Third, it had to create a modern, empathetic impression suggesting an understanding of real people in the real world, thus avoiding "Establishment" images of condescension and indifference. Fourth, it had to appeal to all age groups and to all sectors of society, including all social class groups. Finally, it had to be capable of being promoted with long lasting impact in the media.

The umbrella concept chosen to fulfill these requirements was "Be All You Can Be," selected from among 40

alternatives suggested by the advertising agency responsible for developing the campaign. Initial research carried out by the ARU (G. B. Hastings and D. S. Leathar, unpublished data, 1984) showed that this concept was wide ranging and diverse, and potentially capable of covering several health dimensions, such as positive health, health and fitness, and mental well-being. By being wide ranging and covering many dimensions, however, the umbrella concept ran the risk of not communicating specifically enough about any single component of health. It was believed that its effect would therefore be maximized if it were used with a subsidiary statement to clarify its precise meaning. It could, for example, be combined with the line, "Go for Good Health," if good health was the objective, or "Make the Most of Yourself" if mental well-being or self-fulfillment was the objective. It could also be developed sequentially over time, if desired, by incorporating other subsidiary statements. In addition, the "Be All You Can Be" concept was flexible in situations requiring different emphasis. It could thus be the main component to which subsidiary, topic-specific information was appended, or could itself act as a subsidiary "by-line" in more problem oriented campaigns. Finally, and somewhat unusually in health education, the concept appealed to all age groups and sectors of society; despite initial professional reservations, it was not perceived as middle class or pejorative.

The campaign was launched in the Scottish media in September 1984, with secondary advertising begun in early 1985. The prime components were a 60-second and a 30-second television commercial. Figure 2 shows the final frame from the first of these.

Initial response to the campaign was assessed by placing questions in an omnibus survey (System Three Scotland Omnibus, unpublished data, 1985). (An omnibus is a regularly repeated survey conducted by some commercial agencies on a range of topics. Questionnaire space and data processing facilities are offered to interested clients on a cost per question basis.) This covered a representative sample of over 1,000 Scottish adults, and involved multistage sampling. First, 40 parliamentary constituencies were selected at random using stratified sampling to ensure representativeness in terms of geographical location and political affiliation. Second, one sampling point within each chosen constituency was selected randomly using the electoral roll. Finally, individual respondents were approached following a random route procedure. The results indicated that campaign awareness was high (66%) and appeal broad (72% of those who had seen "Be All You Can Be" felt it was targeting everyone), although slightly skewed towards the young. The campaign was also seen as intending to promote messages about health being enjoyable, taking an interest in health, and leading a full life (see Table 1), and as being successful in this. Attitudinal data showed that 90% of those aware of the material agreed that "it is a warm and friendly way of talking to people about their health," with 81% agreeing that this "made a nice change from health messages that tell you *not* to do things all the time."

FIGURE 2. Final frame of 60-second television commercial launching the "Be All You Can Be" campaign.

TABLE I. Omnibus Survey Results Concerning the "Be All You Can Be" Campaign Message

Prestated Message	Percent Agreeing that This Is the Intended Message (N = 701)	Percent Agreeing that This Message Is Actually Communicated (N = 701)
Suggest that healthy activities can be fun	98	97
Encourage people to take a greater interest in their own health	97	95
Encourage people to live fuller lives	94	92

Positive Nonsmoking Revisited

These findings provided considerable encouragement to SHEG's antismoking campaign team, confirming the appeal of a positive approach and indicating that the "Be All You Can Be" concept had potential as a vehicle for this kind of message. The next step was therefore to produce a new, positive nonsmoking commercial incorporating "Be All You Can Be."

The first attempt to do this targeted adolescents, basing the message on a popular teenage music program called "The Tube." The message was largely concerned with reasons for not smoking, but ended with the caption "Let Your Body Breathe, Be All You Can Be."

Response to the commercial among the target audience was mixed (S. Squair and G. B. Hastings, unpublished data, 1984). The Tube was a very popular, almost cult, program that provided a strong and very positive setting for the commercial. The final slogan was also well received, in much the same way as "No smokers breathe easy" had been, but in this instance interlocking the slogan with the "Be All You Can Be" theme introduced a crucial element of credibility. This suggested that the commercial had the potential to become a powerful positive nonsmoking commercial. However, the rest of the commercial's message, with its emphasis on reasons for not smoking, was too negative and directive for this potential to be realized.

SHEG learned three important lessons from this project. First, the "Be All You Can Be" theme can be at-

tached to a specific antismoking message, and has the potential to lend credibility to positive approaches in this area. Second, the approach must be positive in terms of message as well as style. Third, an otherwise negative message cannot be converted into a positive one simply by adding "Be All You Can Be."

Work on SHEG's latest smoking commercial, which again targets adolescents, is based on this experience. It builds on two of the positive elements of the Tube commercial: the slogan "Let Your Body Breathe" and the connection with the "Be All You Can Be" theme. Both are presented in relation to another positive concept, that of individuality and strength of mind. Thus the complete message is: "Know your own mind about smoking and make the decision to let your body breathe; this will help you to 'be all you can be.' "

Concept boards based on this theme have been developed and tested with target group members, and initial response has been encouraging. The material appears to have the potential to be a relevant and credible positive nonsmoking commercial. It is relevant because it concerns an important issue for potential recruits to smoking, that of resisting pressure to take up cigarettes. It is positive because it emphasizes the decision to "let your body breathe" rather than to reject smoking. Finally, it is credible because of its connection to the "Be All You Can Be" theme. The only apparent weakness is that, because it centers on a reason for not adopting smoking, and is of little relevance to established smokers, its appeal is limited to new or potential recruits to the habit. These initial results suggest that SHEG's goal of an effective positive nonsmoking message may at last be in sight.

Conclusion

The evolution of antismoking publicity in Scotland has been characterized by a deliberate move away from hard-hitting negative approaches and in recent years has largely consisted of a search for an effective means of promoting positive messages about not smoking. This process of change has been mirrored by developments in health education as a whole. Increased interest is now being shown in positive health promotions and in the idea of self-empowerment.[4] The "Be All You Can Be" concept clearly fits this approach. We will leave it to the reader to decide whether Scotland has led or followed the world in this area.

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The Scottish Epidemic

Estimated annual deaths from smoking in Scotland

	Men	Women
Ischaemic Heart Disease	2512	1567
Lung Cancer	2664	396
Bronchitis and Emphysema	854	220
Total deaths due to smoking		8213
Total deaths from all causes	63299	

Estimated annual admissions to hospital of residents of Scotland as a result of their smoking

	Men	Women
Ischaemic Heart Disease	3703	1749
Lung Cancer	5466	853
Bronchitis and Emphysema	2855	1148
Total admissions due to smoking	15774	

Every day 772 constituents will, as a result of the three main diseases caused by smoking, occupy a hospital bed which could otherwise be used for the treatment of other patients. This represents a total cost of £5848076 per year in salaries for nurses and junior medical staff. It does not include consultant salaries, hospital running costs, community, ambulance or primary care costs.

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Cigarette smoking: A "chosen" risk

PASCAL JAMES IMPERATO, MD, GREG MITCHELL

It has been more than 20 years since the surgeon general identified smoking as the nation's most significant source of preventable illness and premature mortality.[1] Today, the annual death toll—perhaps 350,000 people—exceeds the number of American lives lost in battle in World War II.[2,3] Yet over 30% of American adults (and 20% of youths aged 12 to 17) smoke. For them, smoking is an acceptable risk.

Over 50 million Americans smoke and impose their chosen risk on millions of others who involuntarily inhale the toxic components of burning cigarettes.[4] The medical, scientific, and statistical evidence that smoking is bad for health is overwhelming and convincing beyond the shadow of a doubt—except to industry trade groups, such as the Tobacco Institute, which have a vested interest in seeing that people continue to smoke.

Why do so many Americans choose to expose themselves to this rather serious risk to their health? Are they misinformed or uninformed about the risks, oblivious to the warnings, or simply seduced by slick advertising?

One thing is certain: It is a myth that, in regard to deleterious health effects, smokers have "heard it all before." A Federal Trade Commission report noted that about half of all smokers have still not accepted the proposition that "cigarette smoking is dangerous to your health" and can cause lung cancer. The report stated that there is even less general acceptance of smoking's link to specific health consequences such as emphysema and heart disease. Seen in this light, R.J. Reynolds' controversial advertising campaign, which started in early 1984 and called for an "open debate" on the unsubstantiated perils of smoking, was far shrewder than many gave it credit for.[5]

The individual decision to smoke and to continue doing so arises from a web of personality traits, perceived needs, and external influences.

Adult smokers, when compared with nonsmokers, tend to be "risk-takers" who are extroverted, compulsive, defiant. They are more likely to be divorced or separated. They consume more alcohol and coffee than nonsmokers; they take more psychoactive drugs. Housewives are more likely to smoke than working women; blue-collar male workers smoke more heavily than their white-collar counterparts. Among teenagers, those who smoke are more likely to have family and friends who smoke; they are more outgoing and rebellious.[6,7]

Extensive research has found roughly six distinct reasons why people smoke. Some people are stimulated by cigarettes, and feel that they help them "get through the day." For many, cigarettes act as a tranquilizing agent, a crutch that helps them handle personal problems. Others find satisfaction in simply handling cigarettes because they have a strong need to keep their hands busy. About two thirds get real "pleasure" out of smoking; they find that smoking reduces their negative feelings and makes them "feel good." There are also those who are psychologically addicted to smoking, and finally a number of people who simply smoke out of physical habit. (Among young people, peer pressure is a strong force promoting smoking, since many want to be "one of the crowd.") A person may smoke for any one or a combination of these reasons. Studies show that women tend to smoke mainly to reduce anxiety, while many more men smoke purely for "pleasure."[7,8]

Those who are stimulated by cigarettes or simply like handling them find it relatively easy to stop smoking. So do those who get pleasure from cigarettes, provided they have carefully thought about the harmful effects of smoking. People with a craving or psychological addiction to cigarettes and those who use them as a crutch have a hard time quitting, as do habitual smokers.

Nonetheless, as the surgeon general's 1982 report on smoking and health pointed out, people can quit if they try hard enough. Ninety-five percent of those who have successfully quit have done so without organized programs. And it appears that stopping "cold turkey" is more effective than cutting down gradually.[8]

Most people quit either because they are suffering from some serious consequence of smoking or because they have finally responded to the medical warnings. It has been found that brief and simple advice from a doctor is potentially the most cost effective way of getting people to quit. On the other hand, some studies indicate that human decisions are not focused on final outcomes (in this case lung cancer, emphysema, and so forth) but rather on incremental stages. People move ahead one step at a time, regarding what lies several steps ahead as irrelevant. Thus, stressing the long term consequences of smoking to

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young people is not very effective, because these consequences seem too remote; most young people who smoke know many others who smoke, while few know anyone suffering from lung cancer. Lung cancer, emphysema, and the other serious diseases caused by smoking look like low probabilities from where they stand: on the adventuresome side of 40.

Other studies have shown that adults habitually tolerate risks even if they mean a great potential loss—provided that the *probability* of that loss is low. Thus, the health consequences of smoking, taken on their own, are seen as serious but of low probability, and many people are willing to take the risk.

Contributing to the problem is the Tobacco Institute's seductive and reassuring advertising, which effectively dilutes the warnings issued by the surgeon general and others. The Institute has regularly been able to muster some scientific support to its side, successfully conveying the erroneous impression that scientists are evenly split on the subject of smoking and its dangers. This, in turn, lulls many smokers into believing that the final word is not in yet on the link between smoking and lung cancer, or some other risk. Then, too, many smokers believe that their choice is between cigarettes and frayed nerves—or dying at age 81 instead of 82—and so they continue to smoke.

Moreover, although some smokers have switched to filtered cigarettes or to brands low in tar and nicotine as the medical evidence againt smoking has mounted, this is often only a halfway measure at best.

The tar and nicotine content of cigarettes has long been a focus of concern for medical researchers. To combat bad publicity, cigarette manufacturers reduced the tar and nicotine content of cigarettes by an average of almost 50% between 1955 and 1975. Today, more than 50% of the cigarettes sold in the United States have a reduced tar and nicotine content.[9]

People who smoke low tar and nicotine cigarettes often compensate for the reduced levels of these ingredients (which they crave) by increasing their consumption, thus canceling out whatever benefits low tar and nicotine cigarettes provide. Another study found that half of those who smoke low tar cigarettes admit to blocking the filter vents which are supposed to dilute the smoke.

Smoking and Health

How dangerous is cigarette smoking? In 1982 about 111,000 people died of lung cancer, and an estimated 85% of these deaths were directly due to smoking. Lung cancer killed 80,000 men and 31,000 women, reflecting lower cigarette use among women. But women have been smoking cigarettes in increasing numbers. The increase in smoking in recent years among young adult (20–24-year-old) females reflects the relatively sharp rise in smoking among teenage females during the mid to late 1970s. This trend has now been reversed. Over the past two decades, a major pattern in smoking behavior has been the convergence of the proportion of smokers in each of the sexes and age groups. There is now almost no difference in the proportion of smokers between young adult males and females.[4] There is, however, some good news in the statistics. Between 1976–77 and 1984 there was a 35% reduction in the number of high school seniors who smoked. Between 1983 and 1984 the reduction was of the order of 12%.[4] This may reflect the effectiveness of education and information campaigns focusing on the dangers of either starting to smoke or continuing to smoke.

Based on extensive scientific data, we know that those who smoke more than a pack a day have three or four times the general cancer death rate of nonsmokers. For smokers, the lung cancer risk is eight to 15 times that for nonsmokers.

Seen in another way, the statistics tell us that a 25-year-old man who smokes 20 cigarettes a day cuts his lifespan by 4.6 years. If he smokes 40 or more cigarettes a day his lifespan is reduced by 8.3 years. It is estimated that every cigarette smoked reduces the lifespan by 5 ½ minutes—just slightly less than the time spent smoking it.

In February 1982, Surgeon General C. Everett Koop, making an annual report on smoking and health, went further in linking cancer other than lung cancer to smoking. He reported that cigarette smoking is now believed to be a contributing factor in cancer of the urinary bladder, pancreas, and kidney, and that it may be associated with stomach cancer. Many medical scientists think that the ultimate cause and effect relationships between these cancers and cigarette smoking will eventually be demonstrated.[10]

The Tobacco Institute's response to these statistics and to the carefully designed studies upon which they are based was consistent with its past positions. The Institute maintained that whether smoking causes cancer is still an open question and stated that the surgeon general's latest conclusions were not new. This implied that there was nothing urgent or alarming in the surgeon general's report and hence no cause for the government to take stronger antismoking action—or for smokers to stop smoking.

Cancer is not the only increased risk associated with smoking. Smokers are 1.5 to 2.0 times more likely to die of coronary artery disease than nonsmokers. (Smokers who stop immediately reduce their coronary risk by half.) Cigarette smoking is responsible for up to 30% of all heart disease deaths in the United States—about 170,000 a year.[3]

Trends in Cigarette Smoking

The medical and scientific testimony against smoking has been blaring for more than two decades. Why have over 30 million Americans stopped smoking only recently? Why do 90% of all smokers say they would like to quit?

Certainly, the physical fitness craze has had a great deal to do with it. New quit-smoking programs have proven increasingly effective (although up to 75% of those who quit eventually suffer a relapse). But perhaps most significantly, smoking's social standing has suffered; in some circles it is no longer even acceptable to smoke. And among young people it may no longer be "cool." A University of Wisconsin study released in early 1984 showed that people pictured with cigarettes were ranked by college students as being less sexy, less honest, and less mature than the same people pictured without cigarettes. "My guess is that our culture is changing," said Marshall Dermer, an associate professor of psychology who conducted the study. "Older people have not been exposed strongly to negative aspects of smoking."

Nevertheless, according to most accounts, the number of smokers in the United States is rising by about 1% a year (the same rate applies worldwide) because of increasing population and the steady number of women who smoke. Among smokers the proportion of heavy smokers is actually increasing.

Cigarette Advertising

A major reason for the continued good health of the cigarette industry is that the six major American tobacco companies still control the public debate. They spend about $1.5 billion annually in advertising and promotion, the largest amount spent on any product in this country. (By comparison, the government's Office on Smoking and Health has a yearly budget of about $3.5 *million*.)

Besides increased sales, these expenditures encourage, in the opinion of some observers, relative silence from the print media on the subject of smoking. *Time* and *Newsweek*, for example, receive in excess of $30 million a year from cigarette advertising; neither newsmagazine has printed a cover story on the hazards of smoking since 1970, while devoting covers to AIDS, Legionnaire's disease, and toxic shock syndrome. (The June 6, 1983 issue of *Newsweek* contained one story on nonsmokers' rights—but no cigarette advertising. The tobacco companies had not pulled the ads; *Newsweek* did.)

Cigarette companies have not appeared on television since 1970. This turn of events came after John Banzhaf, director of a public interest group, petitioned the Federal Communications Commission to use the Fairness Doctrine to require television and radio stations to give "equal time" to antismoking ads. The antismoking spots subsequently aired were so strong that the cigarette industry decided to voluntarily remove their ads from TV and radio (resulting in the end of the antismoking messages as well).

But this was not a death blow to the cigarette industry; it was, in many respects, a bonanza. Cigarette companies switched to less costly advertising in magazines and newspapers, avoiding the threat of being met with "equal time" ads. With the money they saved on advertising, they launched a two-pronged promotional effort consisting of corporate philanthropy to cultural and sports organizations and a massive print advertising push.

Suddenly there was a Virginia Slims Tour (tennis), the Marlboro Cup (horse racing), the Kent Ladies Gold Classics, the Winston Team America Series (soccer), the Marlboro British Grand Prix (car racing), and "Camel Scoreboards" in the sports sections of 100 newspapers. The cigarette manufacturers also courted respectability by sponsoring such cultural events as the Salem Spirit Concert series, the New York Kool Jazz Festival, and many art exhibitions. (Philip Morris sponsored the Vatican exhibit at the Metropolitan Museum of Art in 1983.)

At the same time, many of the new cigarette ads in magazines and newspapers and on massive billboards began emphasizing natural beauty—the crashing of waves, snow-capped mountains, and rolling plains. The models who appeared in them seemed to grow increasingly younger and attractive; smoking was "sexy." In all of the ads the smoker was shown in *control*—a subtle but powerful message to the millions of smokers who light up to reduce tension. These ads appealed to young people and those who "think young," and no wonder: The land of cigarette advertising is a dream world bereft of coughing, dirty ashtrays, or cancer.

The surgeon general's warning is included in all of these ads, not in matching color and bold print, but in unobtrusive black and white that detracts little from the ads' impact. "Ultra low tar" and filters are promised along with satisfying taste, implying safety and reward all rolled into one cigarette. None of the ads indicate, of course, what the beautiful people in them would probably look and feel like 20 years hence if they were to smoke heavily. The mountain vistas and seascapes are silent about what has happened to those who long ago heeded the advice, "What are you waiting for? Come and try one." No cigarette ads show smokers with emphysema gasping for breath, or those with lung cancer dying in their hospital beds. Yet these visual images are more relevant to most cigarette smokers than rolling waves and rugged mountains.

Ironically, many ads are aimed at the sports- and fitness-minded. Going after the youth, female, and health-conscious markets in one shot, Virginia Slims put out a full-page offer for a warm-up suit called the Ginny Jogger—perhaps the only fitness ad ever to appear with a health warning from the surgeon general printed at its bottom.

One of the most effective antismoking devices making the rounds in this country tackles one of the industry's advertising themes head-on. The documentary *Death in the West*, made for Thames Television in Great Britain several years ago, has been shown to children in 40 states. It includes interviews with six cowboys who are dying from diseases caused by smoking. One scene shows a man astride his horse in the distance, with the Marlboro theme on the soundtrack; a close-up shot reveals that he has an oxygen tank strapped to his saddle and tubes sticking out his nose.

But, in the final analysis, despite such antismoking propaganda, millions of people choose to smoke. No one forces them to do it.

Passive Smoking

Smoking is a chosen risk. Many people who smoke recognize the risk and respond to those who complain about smoking: "It's my problem. It's none of your business."

But this is not so. What is a voluntary risk for one person is an imposed risk on another.

One form of this imposed risk is involuntary or "passive" smoking—nonsmokers inhaling smoke generated by others. In the 1982 surgeon general's report, Dr Edward N. Brandt, Jr, an assistant secretary of Health and Human Services, said, "Prudence dictates that nonsmokers avoid exposure to second-hand tobacco smoke to the extent possible." Dr Brandt's comment was made in response to evidence produced in three studies that showed that the wives of heavy smokers had a higher risk of developing lung cancer than the wives of nonsmokers.[10]

Passive exposure to cigarette smoke is hazardous because the carcinogenic and toxic chemicals in the cigarette are released into the air unfiltered. One study indicated that a nonsmoker sitting at a crowded, smoke filled bar inhales in one hour approximately the same amount of dimethylnitrosamine, a carcinogen, as that inhaled by someone who smokes about 25 filtered cigarettes.

The tobacco industry has fought every effort that would require them to identify publicly the chemicals added to cigarettes, and for good reason: some 4,000 known compounds are generated by burning cigarettes, including many carcinogens and such substances as vinyl chloride, arsenic, and insecticide residues. All of these, of course, are passed on to bystanders. Radioactive substances are also found in cigarette smoke.[11]

During an interview in 1983 Surgeon General Koop declared that "We are going to prove without any doubt how dangerous" the problem of "second-hand" smoking is to the nonsmoker; recent studies, he said, "showed beyond any shadow of a doubt sidestream smoking is very dangerous to your health." Koop suggested that the warning on a cigarette pack might be more effective if it read: "The smoke from the cigarette you are about to exhale is dangerous to the health of your children." (The Tobacco Institute asserts that the preponderance of scientific testimony does not show that ambient tobacco smoke is harmful.)

Because they consider cigarette smoke annoying—not necessarily *harmful*—nonsmokers have started complaining loudly. A Roper survey found, in 1978, that the percentage of people favoring separate smoking and nonsmoking sections ranged from 61% (for offices) to 91% (trains, planes, and buses). Roper called the nonsmokers' rights movement "the most dangerous development to the viability of the tobacco industry that has yet occurred." (This is shown by the following statistic: If each American smoker smoked just one less cigarette each day, the tobacco industry would lose about half a billion dollars a year.)[12]

Antismoking sentiment is growing more "dangerous" by the year. In 1984 C. Everett Koop startled some observers by calling "a smoke-free society by the year 2000" this country's top health goal. Representatives from the American Cancer Society, American Lung Association, and American Heart Association promptly formed a coalition to take up this challenge. The Tobacco Institute condemned this effort, stating: "The new prohibitionists have no place among a free people."

Aggressive antismoking sentiments inspired a host of new state and city laws, the most comprehensive of which was the state of Minnesota's Clean Indoor Act, which took the radical step of prohibiting smoking everywhere unless it was specifically permitted.[12] Among other things, the law requires no-smoking sections in restaurants.

By mid-1986, some 75 localities around the United States had adopted laws that restrict where people can smoke. In the spring of 1986, New York City's Mayor Edward Koch introduced a smoking restriction bill that is by far one of the most stringent in the country. If passed by the city council it would ban smoking in many "enclosed places" such as stores, taxicabs, public hearing rooms, restrooms, waiting lounges, and semiprivate hospital rooms. The mayor appointed former Secretary of Health, Education and Welfare Joseph A. Califano, Jr to head a review committee that began hearings in May 1986.[13] At the time of this writing, it is unclear what version of this bill will pass.

While people can choose to smoke or not, and to leave rooms or restaurants to avoid cigarette smoke, children and the unborn are defenseless. A number of adverse effects of parental smoking on infants and children have been documented.[14-17]

Another way people who choose to smoke strongly affect nonsmokers is reflected in the following statistics: Estimates of the cost of smoking to society as a whole in the United States range from $35 billion to $49 billion (this includes direct health care costs, lost wages, and decreased productivity). These figures do not take into account what C. Everett Koop calls "something else far worse—the cost of human dignity and quality of life of the families left behind by people who die due to smoking."

By one estimate, every nonsmoking adult in this country pays at least $100 a year in taxes and increased insurance premiums to help cover the health care costs piled up by smokers. Insurance companies have long been criticized for not offering lower life insurance premiums to nonsmokers, who tend to live several years longer than heavy smokers. (Some companies, including Prudential, do offer discounts, and this trend is beginning to extend to health, fire, and even auto insurance.)

Cigarettes and Fires

Smoking, a risk which appears so personal on its face, imperils others in at least one other extremely destructive way: Cigarettes are the leading cause of deaths due to fires. About 65,000 fires every year—around 8% of all residential fires in the United States and about a quarter of all residential fire related deaths and injuries—are smoking related. This translates into 2,300 deaths and 5,800 injuries annually and a property loss of $300 million.[18]

Cigarettes cause fires because, when not being puffed, they can burn for 20 to 45 minutes. A cigarette dropped on upholstered furniture will usually smolder, then flame within 15 minutes. The devastation of cigarette caused residential fires is dramatically depicted in a recent public service message made for television by the New York City Fire Department. The film shows Betty Brinkley, a Camden, New Jersey housewife, who was badly disfigured in a 1977 fire that killed her husband and three children. Brinkley's husband fell asleep while smoking a cigarette.

Yet even tragedies such as this have not inspired a solution: legislation that would mandate self-extinguishing cigarettes. The Tobacco Institute has staunchly opposed these proposed laws, and legislators in several states, including New York and Connecticut, have killed such bills.

The tobacco industry opposes these measures because they would require the use of cigarette papers that would allegedly adversely affect the taste of cigarettes.

Proponents of self-extinguishing cigarettes, however, do not agree that it is "inevitable" that these products would taste worse or contain more tar and nicotine. They point out that cigarettes are already chemically altered—to provide a long, slow burn. And they say that at least two brands sold in the United States—More and Sherman's—have been shown to be more fire safe than others.

The battle lines are now drawn between the tobacco industry and those who want to reduce the risks of cigarette caused fires. The industry is certain to put up a long and hard fight to keep cigarettes burning like fuses, while remaining generous with donations to general fire prevention efforts. (The Tobacco Institute recently donated

$640,000 to the National Fire Protection Association's smoke detector program.)[18] The American Medical Association and the American Burn Association have endorsed efforts to make a safer cigarette but it is unlikely that the federal government will take a strong stand. The government has long played an inconsistent—some would say, hypocritical—role on the smoking issue ever since the surgeon general's 1964 declaration that smoking was dangerous. On the one hand, the government has mandated warnings on cigarette packs to discourage consumption, and on the other it has given generous federal price supports to tobacco farmers.

Health Warnings

In an effort to convince people that the health consequences of smoking are serious and real, health organizations and some members of Congress in 1984 pushed for more specific labels on cigarette packages, and suggested that they be changed regularly (or "rotated"). Many in the advertising field saw the present warning as suffering from "wear out," having become so familiar that it is often overlooked. (One study showed that only one in 50 smokers acknowledged reading it.) Yet the Reagan Administration gave little support to this proposal, and the Tobacco Institute was against it, with good reason: The proposed new labels were much more explicit about the health consequences of smoking.

However, during the spring and summer of 1984, a number of congressional committees gave overwhelming support to strengthening the wording on cigarette packages. Aware that stiff legislation might be passed, the tobacco industry decided to negotiate behind the scenes with health groups and legislators proposing the new laws. (Deleted from the bill and proposed warnings were any references to "addiction.") The Comprehensive Smoking Education Act was finally approved overwhelmingly by Congress in September 1984.[19] Representative Albert Gore of Tennessee, a major sponsor of the bill, said: "This has been a bitter pill . . . for [the tobacco industry] to swallow, but in so doing they have made stiffer punitive legislation less likely in the years ahead." The new warnings that rotate every month read:

- SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy
- SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risk to Your Health
- SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight
- SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide

The bill requires that warnings be 50% larger in advertisements than the old warning. In addition, cigarette manufacturers have to disclose to the secretary of Health and Human Services a list of the additives used in their products.

Surprisingly, some antismoking activists opposed the change in warning signals, on grounds that it would disarm what they feel is potentially the strongest weapon against cigarettes: product liability lawsuits. They feared that tougher warnings would only bolster the tobacco industry's main legal defense: that smokers voluntarily assume all risk by choosing to smoke. (No one has ever successfully sued a cigarette company.) They pointed out that the reason the tobacco industry was so adamant about removing any reference to "addiction" on the labels was that this would seriously weaken their "voluntary risk" defense.

The new warning labels still have to compete with billboards filled with beautiful landscapes and beautiful people, the implied safety of filtered and ultra-low-tar cigarettes, and promises of fresh tastes and satisfactions. Thus, smoking, although a personal decision, is clearly not an uninfluenced one. Those who smoke choose the risks not only from free volition, habit, and need, but also because they have been persuaded, influenced, propagandized, or confused, or because they remain oblivious or ignorant. The choice—while still their own—is not as free as one might think, and it is a choice whose impact is not confined to the individual "freely" making it.

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The British Medical Association's campaign against the tobacco industry

PAMELA TAYLOR

October 16, 1984 marked the start of the British Medical Association's (BMA) campaign to ban the advertising and multimillion-pound promotional activities of the tobacco industry. Journalists were invited to attend a press conference in BMA House, London, in the gracious vault-ceilinged Princes Room. The room had been filled with the promotional trappings of the tobacco industry: poster and magazine advertisements; arts programs and sporting leaflets; blown-up photographs of cigarette promotions complete with enthralled children, their hands outstretched; mannequins dressed in clothes bearing tobacco company logos; and a continuous slide show of shop window advertising displays.

"The BMA believes all the promotional material in this room should be made illegal," declared BMA Secretary Dr John Havard to the journalists. Dr John Dawson, head of the BMA's Professional Division, explained that the aim was "to cut through the millions of pounds spent by the tobacco industry to disguise what their products really are. They are trying to buy an acceptable face for a product in a way which we say should be made illegal."

Why did it take the BMA so long to launch its campaign? After all, as early as 1950 Doll and Hill had warned in the *British Medical Journal* that "smoking is a factor and an important factor in the production of carcinoma of the lung."[1] The Royal College of Physicians of London highlighted the dangers of smoking in 1962[2] and the United States' Surgeon General's report[3] concluded in 1964 that "Cigarette smoking is a health hazard of sufficient importance in the United States to warrant remedial action."

British campaigners such as the Health Education Council and Action on Smoking and Health (ASH)[4] battled with budgets a fraction of the size of that of the wealthy tobacco companies, and without the help of the BMA. In fact, representatives of ASH and the BMA had never even formally met. The BMA's annual representative meeting, the 600-strong physicians' parliament, had been passing resolutions opposing the tobacco industry since 1965, but still the BMA took a back seat. The majority of British physicians, unaware of the politics surrounding the tobacco industry in Britain and around the world, naively believed that the government would forget its dependence on the £11.5 million (approximately $18 million) in tax paid by smokers each day, and would find the necessary parliamentary time and will to legislate. Some physicians wrote to me opposing the launch of the BMA's campaign, claiming that being right and being patient were enough.

The BMA has a fine history of campaigning, dating back to the 1850s. Today, successful campaigning means sophisticated press and parliamentary techniques and a sound network of physicians to take action locally. Recent campaigning victories, such as the introduction of legislation making seat belt wearing compulsory for front seat passengers, is evidence that the BMA is now ready to take on what has been described as "probably the most insidiously powerful lobby in the country."[4]

THE BRITISH MEDICAL ASSOCIATION'S CAMPAIGN

BMA Secretary John Havard agreed that the time was right, and nine months of research led up to that October press conference. Intensive parliamentary lobbying enabled the categorization of every Member of Parliament (MP) into "for," "against," and "do not know." The "against" list was very long, with most MPs on it using what has been dubbed "tobacco speak." Years of tobacco company champagne receptions at the opera and key sporting events, financial briefs on revenue and jobs, and 365 televised hours a year of tobacco sponsored sporting events all added up when it came to forming MPs' opinions.

A special edition of *BMA News Review* was planned to coincide with the press conference. *News Review* is a monthly magazine of medical politics published by the BMA, and the editor made it a publication that enabled physicians to learn how to help the campaign. The politics of the tobacco industry and clinical aspects of smoking were covered, but most important, one article recommended local action that physicians could take to help the campaign. The issue told physicians how to write to MPs and send letters to the press, and how to put pressure on local authorities to ban cigarette advertising. Finally, there was a coupon for physicians to fill in if they wanted to join the movement and campaign actively. The response was overwhelming, and the campaigning physicians augmented the work carried out by the 180 physicians who

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were elected honorary press and parliamentary campaigners around Britain.

Early in the campaign, the BMA wanted to find a way of impressing on MPs the number of deaths from tobacco related diseases. It was important to make the MPs think of their constituents. One hundred thousand British deaths a year—or 270 a day—had to count for something. Thousands of black-edged postcards were produced for physicians to send to their MPs each time a patient died of a smoking related disease. The patients' names were kept confidential, but the causes of death—lung cancer, chronic obstructive lung disease, coronary heart disease, and other tobacco related cancers or vascular diseases—were listed on the black-edged card; physicians simply had to mark the appropriate box and send the card to the House of Commons.

In any long term campaign, it is essential to have short, medium, and long term goals. A campaign plan covering a ten-year period was drawn up. The prelaunch research months were crammed with short term goals, the first year was mapped out in minute detail, and, spread over the years, medium and long term targets were written in. Regular office meetings ensured a continuous assessment of progress toward achieving these goals.

MPs remain a high priority. One has to show them that the majority of their constituents—the people who vote for them—want action. For too long, too many MPs had readily accepted the tobacco industry line. On November 26, 1985, the BMA joined with the Health Education Council to launch "The Big Kill,"[5] a 13-volume document listing tobacco related deaths by parliamentary constituency and detailing the cost to the National Health Service. At the televised press conference, black balloons were released into the sky to mark the number of deaths that day caused by smoking. The results were impressive. In its longest editorial since the Falklands crisis, the London *Times*[6] called for legislation to phase out tobacco advertisements and sponsorship, stating, "It is no longer enough just to say that smoking is declining and can be left to die out at its own rate. It is the industry that should be dying more quickly, not the customers." "The Big Kill" also provided local campaigners with the data they need to work toward banning local tobacco advertisements and sponsorship.

In any campaign, the national press is a vital target. The medical correspondents of Britain's national newspapers were well aware of the clinical evidence against smoking, but what the BMA had to do was to build on the work done by ASH and others, making the journalists aware of the politics of the tobacco industry. Included in the campaign timetable was a major media event each month. For these, the BMA relied heavily on newfound friends who were seasoned campaigners in the field. For example, Dr Frank Ledwith, a research fellow at Manchester University, carried out some revolutionary research on 880 school children.[7] He concluded that tobacco industry sponsorship of sporting events acted as advertisements to children. Children preferred to smoke the brands they saw associated with television sports sponsorship. Dr Ledwith announced the results at a press conference at the BMA.

Simon Chapman from Australia's National Health and Medical Research Council was able to advise us on action based on his experiences in Australia. He also wrote for us a booklet concerning the tobacco industry's arguments for advertisements. Launched at a press conference and sent to every MP, it has now become a source document used regularly by the BMA and other campaigners. We plan to revamp it and issue an accompanying booklet on sponsorship.

The exploitation of women by the tobacco industry—manifested by the introduction in the UK of brands aimed at women coupled with massive advertising campaigns in women's magazines—was dealt with by Drs Bobbie Jacobson and Amanda Amos, who wrote *When Smoke Gets in Your Eyes*.[8] The authors meticulously surveyed 53 British magazines for cigarette advertising and health coverage and presented their findings against a background of what they described as "the rising female death toll from cigarette smoking, the slower decline of smoking among women, and the rising proportion of girls smoking." The report contained recommendations to the government, the tobacco industry, magazines and editorial staffs, health professionals, and the general public. The advertising industry was suitably strident in its attempts to defend itself, but IPC, the biggest women's publishing group, revised its advertising policy—a crucial victory.

No high-profile campaign can progress for long without a battle, and the BMA provoked a major row when it published a report on investments in the UK tobacco industry.[9] The report listed shareholdings in tobacco companies held by health agencies, educational establishments, churches and related organizations, and welfare agencies. The press conference made the lead story on the national television news, and many institutions with which the BMA had worked for decades were angry at these apparently ill-mannered tactics. The BMA asked those organizations with investments in the tobacco industry either to sell or to use their power as shareholders to press for diversification out of tobacco. Regional and local newspapers made sure the story kept running.

Lobbying in the House of Commons

In the House of Commons lobbying by the BMA continued, with long lists of official Questions to Ministers. All the information was analyzed and used to keep the BMA's political profile up to date. It was now time to risk a debate in the Upper Chamber, the House of Lords, where BMA President Lord Pitt of Hampstead introduced draft legislation to ban cigarette advertising. The purpose of this action was to test the organizational skills of the tobacco industry and to learn from that experience. The BMA was annihilated, but it learned a lot.

In the Lower House—the House of Commons—draft legislation to phase out sports sponsorship, introduced by Conservative MP Roger Sims, was not even debated. An anonymous MP merely called "object," and that was the end. Still, it was a learning experience, and eight months later Roger Sims introduced that same draft legislation, this time forcing a debate. The BMA even stimulated national press coverage by holding its first-ever press conference at the House of Commons on the eve of the hoped-for debate. For the first time, the BMA deliberately bypassed the medical journalists and took the argument to the general press.

There are many occasions during a campaign when other groups and individuals come forward with offers of help. It is important for an organization as powerful as the BMA not to attempt to stifle their individuality, taking over the ideas as its own. Such action would soon discourage others from coming forward and, just as important, the public, press, and Parliament would not be given the opportunity to see the full range of concerned organizations. One group that came forward was Artists' Campaign Against Tobacco Sponsorship (ACTS). They launched their organization at the BMA when *BMA News Review's* editor commissioned an article by the former secretary general of the Arts Council, Sir Roy Shaw. Later, ACTS joined with stars from BBC television's top-rated children's show to present a larger than life facsimile of a full-page advertisement placed by the BMA in the London *Times*. The advertisement called on the Chancellor of the Exchequer to increase the tax on cigarettes to deter children from smoking. The advertisement cost £12,500 ($19,133), and 200 organizations contributed from £10 ($15) to £5,000 ($7,653) each to appear in the list of supporters. It was the biggest collection of medical organizations ever to make a statement.

In addition to activities in Parliament and in the press, the BMA has used its ability to contact ministers to arrange meetings on various aspects of the campaign. High level deputations, often led by the BMA's Chairman of Council, have met with ministers responsible for health, sport, and finance, and this aspect of the campaign will continue.

It is important to pick up even the smallest changes in attitude in Parliament, the press, the public, and among opinion formers. Those much needed changes are taking place. Journalist Peter Taylor noted in the revised edition of his book *The Smoke Ring*,[10] "The significance of the BMA's campaign is that it is political."

Draft Legislation

A major breakthrough in the campaign is the progress of draft legislation to stop the sale of tobacco products to children under 16 years of age. This proposed legislation includes the sale of Skoal Bandits chewing tobacco, an American-imported phenomenon unheard of here until the factory was opened in Scotland in July 1985. For the first time, physicians and dentists protested in the streets, and Scottish union officials said that workers preferred unemployment to jobs created to manufacture a carcinogenic product. Alison Hillhouse of the Scottish Committee for Action on Smoking and Health coordinated the opposition, aided by interested physicians.

Scottish MP John Home Robertson has made history by taking his draft legislation on the sale of tobacco products to children into the committee stage, the stage where MPs consider the draft in detail. No anti-tobacco measure has progressed this far before.

Television Exposure

The attitudes of television program makers have also changed. While one or two programs still covered the subject, most program makers looked bored at the idea of yet another item on smoking. They argued that everyone knew of the harmful effects of smoking, and that there was nothing new to say. Now, however, the BMA's press office is kept busy providing physicians to appear on television and, for the first time, audiences are voting to ban advertising and sponsorship by the tobacco industry.

The Campaign Continues

Even health professionals have changed the nature of their conferences. Exchanging clinical information on smoking will always be, and must be, the priority, but this year saw the first conference on the political aspects of tobacco, organized by Health Education Services in Cambridge. The television industry and the national press were quick to see the significance of this.

The government's Chancellor of the Exchequer in his budget speech[11] cited the evidence he had received on health grounds as his reason for increasing the cost of cigarettes above the rate of inflation.

Creating a society in which children are able to grow up free from the daily pressures they now endure to start smoking remains the aim of the BMA. Children, young people, and adults who are addicted to nicotine should have the freedom to go about their daily lives without interference by the multimillion-pound promotional activities of the tobacco industry. The voluntary agreements between the government and the tobacco industry have been described by the BMA as "a sick joke." The campaign for legislation will continue. And, as BMA Secretary Dr John Havard said, "As doctors we must all now speak out or be guilty of collusion."

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9. Gilbert D: *Report on Investment in the UK Tobacco Industry*. London, BMA Professional Division, 1985.
10. Taylor P: *The Smoke Ring: Tobacco, Money and Multinational Politics*, rev ed. New York, New American Library, 1985.
11. Hansard, House of Commons, March 18, 1986, col 180.

Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

The war against smoking

TO THE EDITOR: The war against smoking is not yet over, but more and more battles are being won. Cigarette smoking, once looked upon only as a nasty habit, is now considered socially unacceptable. Smokers feel unwanted, undesirable, and in some instances even ostracized.

It seems almost incomprehensible that even though the public has always known that inhaled toxic fumes from cigarettes can cause lung cancer and heart disease, it was not until smokers were sequestered in the back corners of restaurants, and prohibited from puffing their smokes in the supermarket, that they became convinced that there were some very good reasons for giving up the habit.

There is another very good reason—cost. Congress has just renewed the 16-cent-per-pack tax, after hearing convincing evidence that increased cost does indeed cut down consumption. This especially affects young people, particularly young girls. It is they, unfortunately, who are lured into smoking addiction by seductive cigarette advertising.

The U.S. Surgeon General, Dr C. Everett Koop, in his personal war against cigarettes, has called for a totally smoke-free environment by the year 2000.[1] Up until now several battles have been won: the continuation of a stiff federal tax on cigarettes, and the restriction or banning of smoking in the workplace and in public buildings. At least two more major confrontations with tobacco industry lobbyists lie ahead: the elimination of the tobacco subsidy, and the prohibition of cigarette advertising in magazines and newspapers.

When, by the year 2000, these additional battles are won, Surgeon General Koop will be able to announce to the people of America that the final victory is ours.

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1. Koop, CE: A smoke-free society by the year 2000. *NY State J Med* 1985; 85:290–292.

Smoking as hazardous conduct

TO THE EDITOR: The smoker of cigarettes is constantly exposed to levels of carbon monoxide in the range of 500 to 1,500 parts per million when he or she inhales cigarette smoke.[1]

The Occupational Safety and Health Act of 1970, 29 USC 651-678, forbids hazards. Rules such as 29 CFR 1910.1000.Z provide specific examples of hazards such as carbon monoxide (a limit of 50 parts per million). An employer has a duty to prevent and suppress hazardous conduct by employees.[2] Compliance with 29 CFR 1910.1000.Z is mandatory, not optional. Relative to smoking, an employer must comply with the "duty to prevent and suppress" a hazard such as carbon monoxide, since "the detrimental effects of cigarette smoking on health are beyond controversy."[3]

The so-called nonsmokers' rights movement is in a sense misdirected on this issue, although accurate, albeit by indirection. As a matter of law, it is not necessary to reach the issue of the hazard to nonsmokers, as the employer's duty to prevent and suppress hazardous conduct arises when smokers endanger themselves, a point in time *before* additional personnel (such as nonsmokers) are also endangered. So-called nonsmokers' rights cases such as *Shimp v New Jersey Bell Telephone Co*, 145 NJ Super 516, 368 A2d 408 (1976), and *Smith v Western Electric Co*, 643 SW2d 10 (Mo App 1982), were improperly pleaded. They addressed matters other than the hazard to smokers themselves, although the cases arrived at the right result—suppression of hazardous conduct.

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2. *National Realty and Construction Co, Inc v Occupational Safety and Health Review Commission*, 489 F2d 1257 at 1266, n 36 (DC Cir 1973).
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Cigarette smoking in perspective

TO THE EDITOR: The December 1983 and July 1985 issues of the *Journal* demonstrate profound editorial knowledge about the problems created by smoking, and the editors should be commended for magnificent productions. None of the material is new, as it has been said and written many times. However, repetition is the essence of education, and perhaps the human race can be taught the dangers of smoking. And yet, I have an uneasy conviction that the sermon is being delivered to deaf parishioners and the seed is being sown on stony soil where it grows without root and is blown away. All of your good people have huffed and puffed but the brick house built by the American tobacco companies is firm, secure, and not about to be destroyed.

The problems engendered by smoking may be comparable to the difficulties created by alcohol, hard drugs, handguns, and automobiles. Sadly, the major proportion of all of these problems is correctable. I recall for your readers that more than 19,000 people were killed by gunfire in this country in the last year for which statistics are available, and that 53,000 individuals lost their lives on the highway through automobile misuse. Reliable information about illicit drug use is difficult to obtain, but estimates of victims of opiate dependence vary from 400,000 to several million individuals. In New York City alone, more than 1,000 deaths occur annually from heroin abuse. The desolation visited upon victim and family from the use of alcohol and hard drugs defies measure.

The economic contribution of the tobacco industry to the general tax structure is great. An annual tax of $6 billion

payable to the federal, state, and local governments is a strong reason for lack of restrictive action. The contribution of the alcohol industry likewise is also substantial. Smoking indeed creates a nasty health problem throughout the world, but can we forget the greater number of difficulties induced by these other agents?

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Clean indoor air

TO THE EDITOR: The Monroe County legislature is about to consider a Clean Indoor Air law that will protect people from exposure to tobacco smoke in public places. As physicians interested in maintaining the health of our community, we enthusiastically support the passage of a precisely written, strictly enforced Clean Indoor Air Act.

Cigarette smoking is the most significant preventable cause of disease in the United States. The hazard of smoking to smokers themselves is beyond debate. It is estimated that over 350,000 people die each year of diseases that are related to cigarette smoking, including lung cancer, emphysema, and coronary heart disease.[1,2] There is also growing concern that passive or secondhand smoking due to involuntary exposure to tobacco smoke may have adverse health effects on the nonsmoker, as well. The smoke of cigarettes contains known carcinogens. Metabolites of this smoke can be demonstrated in the urine of the passive smoker, indicating that the smoke has been inhaled. Although it is difficult to assess the exact risk of such exposure, I think there is adequate reason for concern. Some of the population studies that have been done indicate that there is an increased risk of lung cancer in persons passively exposed to high levels of cigarette smoke. Further, evidence suggests that passive exposure of children to cigarette smoke results in an increased incidence of lung disease. Patients with asthma and coronary artery disease may have their conditions worsened by involuntarily inhaling tobacco smoke. Many people find tobacco smoke irritating to the eyes and nose.

In Monroe County, New York, it is estimated that 78% of the adults are nonsmokers (based on unpublished survey data, Monroe County Department of Health). I think that the right of people to clean indoor air must be protected. Those who are addicted to smoking and wish to stop should have the support of their physicians. As to those who wish to continue smoking despite the health concerns, I think that their smoking must be confined to areas where it will not adversely affect the rights of others to clean air.

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1. Smoking and cancer. *MMWR* 1982; 31:77–80.
2. Smoking and cardiovascular disease. *MMWR* 1984; 32:677–679.

ERRATUM

Reference 2 of the article, "A proposed solution to the malpractice issue" (1986; 86:394–395) should have identified the Chairman of the Assembly Republican Task Force on Health Fraud and the Elderly as Peter Sullivan (not Peter Herbert).

MSSNY Medical Liability Reform Fund Honor Roll

In the September 1985 issue the *Journal* began publishing the list of physicians who have generously contributed to the campaign to inform the public about the crisis in medical liability litigation. The names of additional contributors are listed below.

Sallah Uddin Abbasey, MD
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Irving Abelow, MD
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AIDS

The Management of AIDS Patients. Edited by David Miller, Jonathan Weber, and John Green. 202 pp, illustrated. Dobbs Ferry, NY, Sheridan House, Inc, 1986. $24.50 (paperback)

AMBULATORY CARE

Principles of Ambulatory Medicine. Second Edition. Edited by L. Randol Barker, MD, John R. Burton, MD, and Philip D. Zieve, MD. 1494 pp, illustrated. Baltimore, Williams & Wilkins, 1986. $82.50 (hardcover)

CARDIOLOGY

Cardiac Arrhythmias: Self-Learning. Companion volume to **Manual of Cardiac Arrhythmias.** By Edward K. Chung, MD. 200 pp, illustrated. New York, Yorke Medical Books, 1986. $30.00 (hardcover)

Clinical Doppler Echocardiology. By José Missri, MD. 256 pp, illustrated. New York, Yorke Medical Books, 1986. $45.00 (hardcover)

Manual of Cardiac Arrhythmias. By Edward K. Chung, MD. 307 pp, illustrated. New York, Yorke Medical Books, 1986. $30.00 (hardcover)

Manual of Exercise ECG Testing. By Edward K. Chung, MD. 178 pp, illustrated. New York, Yorke Medical Books, 1986. $30.00 (hardcover)

GERIATRICS

Growing Old, Staying Young. What Medicine and Science Are Doing to Make Aging a Natural Part of a Healthier and Longer Life. By Christopher Hallowell. 309 pp. New York, William Morrow & Co, 1985. $17.95 (hardcover)

HEALTH CARE

America's Health Care Revolution. Who Lives? Who Dies? Who Pays? By Joseph A. Califano, Jr. 241 pp. New York, Random House, Inc, 1986. $17.95 (hardcover)

Heal Thyself. The Health of Health Care Professionals. Edited by Cynthia D. Scott, PhD, and Joann Hawk, PhD. 336 pp, illustrated. New York, Brunner/Mazel Publishers, 1986. $30.00 (hardcover)

HEMATOLOGY

Blood Disorders. The Facts. By Sheila T. Callender. 164 pp, illustrated. New York, Oxford University Press, 1985. $13.95 (hardcover)

HISTORY OF MEDICINE

Sixteenth Century Physician and His Methods. Mercurialis On Diseases of the Skin. By Richard L. Sutton, Jr, MD. 226 pp, illustrated. Kansas City, Mo, The Lowell Press, 1986. $37.50 (hardcover)

INTERNAL MEDICINE

A Primer of Water, Electrolyte and Acid-Base Syndromes. Seventh Edition. By Emanuel Goldberger, MD. 414 pp, illustrated. Philadelphia, Lea & Febiger, 1986. $19.50 (paperback)

Pocket Reference for Medical Intensive Care. Edited by Barbara Anne Phillips, MD. 412 pp, illustrated. Rockville, Md, Aspen Publishers, Inc, 1986. $23.50 (softcover)

LABORATORY MEDICINE

Interpretation of Diagnostic Tests. A Synopsis of Laboratory Medicine. Fourth Edition. By Jacques Wallach, MD. 825 pp, illustrated. Boston, Little, Brown & Co, 1986. $18.00 (paperback)

MEDICAL LIABILITY

Confronting the Malpractice Crisis. Guidelines for the Obstetrician-Gynecologist. Edited by Daniel K. Roberts, MD, Jeffrey A. Shane, MD, and Margaret L. Roberts. 304 pp. Kansas City, Kan, Eagle Press, Inc, 1985. $50.00 (hardcover)

Medical Malpractice. A Preventive Approach. By William O. Robertson, MD. 222 pp. Seattle, University of Washington Press, 1985. $20.00 (hardcover)

Medical Malpractice. Theory, Evidence, and Public Policy. By Patricia M. Danzon. 264 pp, illustrated. Cambridge, Harvard University Press, 1985. $25.00 (hardcover)

MISCELLANEOUS

Afraid to Ask. A Book for Families to Share About Cancer. By Judylaine Fine. 178 pp, illustrated. New York, William Morrow & Co, 1986. $12.88 (hardcover)

The Doctor's Guide to You and Your Colon. A Candid Helpful Guide to Our #1 Hidden Health Complaint. By Martin E. Plaut, MD. 138 pp, illustrated. New York, Harper & Row, 1986. $5.95 (softcover)

Employee Support for Employee Caregivers. By the New York Business Group on Health, Inc. 32 pp. New York, The New York Business Group on Health, Inc, 1986. $30.00 (softcover)

From Roots to Late Budding. The Intellectual Adventures of a Medical Scientist. By Andre F. Cournand, MD. 232 pp, illustrated. New York, Gardner Press, Inc, 1986. $19.95 (hardcover)

Handbook of 1985 Living Will Laws. By Society for the Right to Die. 128 pp. New York, Society for the Right to Die, 1986. $5.00 (softcover)

H.E.L.P. The Health Emergency Life-Support Program. Edited by Leon J. Warshaw, MD. 49 pp. New York, The New York Business Group on Health, Inc, 1986. $30.00 (softcover)

Medical Makeover. The Revolutionary No-Willpower Program for Lifetime Health. By Robert M. Giller, MD, and Kathy Matthews. 276 pp. New York, William Morrow & Co, 1986. $16.95 (cloth)

Medical Topography of Upper Canada. By John Douglas. 45 pp. Nantucket, Mass, Watson Publishing International, 1986. $9.95 (cloth)

More The Official Doctors' Joke Book. By Larry Wilde. 181 pp, illustrated. New York, Bantam Books, 1986. $2.95 (paperback)

Poetry As Healer. Mending the Troubled Mind. Edited by Jack J. Leedy, MD. 320 pp. New York, The Vanguard Press, 1985. $14.95 (paperback)

Public Concerns, Community Initiatives. The Successful Management of Nursing Home Consumer Information Programs. Edited by Carol Ewig and John Griggs. 264 pp. New York, 1985. $25.00 (softcover)

Useful Procedures in Medical Practice. Edited by Paul W. Roberts, MD, 610 pp, illustrated. Philadelphia, Lea & Febiger, 1986, $34.50 (softcover)

NEUROPHYSIOLOGY

Circadian Rhythms in the Central Nervous System. Edited by P. H. Redfern, I. C. Campbell, J. A. Davies, and K. F. Martin. 270 pp, illustrated. Deerfield Beach, Fla, VCH Publishers, 1985. $59.50 (hardcover)

OBSTETRICS AND GYNECOLOGY

Cervical Adenocarcinoma: A Colposcopic Atlas. By Minoru Ueki, MD. 73 pp, illustrated. St. Louis, Mo, Ishiyaku EuroAmerica, Inc, 1985. $30.00 (hardcover)

The Cesarean Birth Experience. A Practical, Comprehensive and Reassuring Guide for Parents and Professionals. By Bonnie Donovan. 265 pp. Boston, Beacon Press, 1986. $9.95 (softcover)

Learning About Menstruation. Every Girl. By Helen McKinnon Dian, PhD, and Janice M.

Morse, PhD. 84 pp, illustrated. Toronto, Canada, General Publishing, 1985. $7.95 (paperback)

OB/GYN Emergencies. The First 60 Minutes. Edited by Roy G. Farrell, MD. 341 pp, illustrated. Rockville, Md, Aspen Publishers, Inc, 1986. $37.00 (hardcover)

Practical Obstetrical Ultrasound. By John W. Seed, MD, and Robert C. Cefalo, MD. 198 pp, illustrated. Rockville, Md, Aspen Publications, 1986. $33.50 (hardcover)

ONCOLOGY

The American Cancer Society Cancer Book. Prevention, Detection, Diagnosis, Treatment, Rehabilitation, Cure. By Arthur I. Holleb, MD. 650 pp, illustrated. Garden City, NY, Doubleday & Co, 1986. $22.50 (hardcover)

Colonic Neoplasms. By Hans Elias. 184 pp, illustrated. St. Louis, Mo, Ishiyaku EuroAmerica, Inc, 1985. $30.00 (hardcover)

ORTHOPEDIC SURGERY

Ligament Injuries and Their Treatment. Edited by D. H. R. Jenkins, MB, ChB, ChM, FRCS. 346 pp, illustrated. Rockville, Md, Aspen Publications, 1985. $40.00 (hardcover)

PEDIATRICS

The State of the World's Children—1986. By United Nations Children's Fund. 156 pp, illustrated. New York, Oxford University Press, 1985. $6.95 (softcover)

PHARMACOLOGY

The Antimicrobial Drugs. By William B. Pratt, MD, and Robert Fekety, MD. 501 pp, illustrated. New York, Oxford University Press, 1986. $27.95 (softcover)

PREVENTIVE MEDICINE

The American Cancer Society's "Freshstart": 21 Days to Stop Smoking. By Dee Burton, PhD. 159 pp. New York, Pocket Books, 1986. $3.95 (paperback)

Health Education and the Media II. By D. S. Leathar, G. B. Hastings, K. M. O'Reilly, and J. K. Davies. 262 pp, illustrated. Elmsford, NY, Pergamon Press, Inc, 1986. $49.50 (hardcover)

Travel Healthy. The Traveler's Complete Medical Kit. By Harold Silverman, PharmD. 192 pp. New York, Avon Books, 1986. $3.50 (paperback)

PSYCHIATRY

Existence, Culture, and Psychotherapy. By Clinton R. Meek. 251 pp. New York, Philosophical Library, Inc, 1985. $19.95 (hardcover)

The Fifteen Minute Hour. Applied Psychotherapy for the Primary Care Physician. By Marian R. Stuart, PhD, and Joseph A. Lieberman III, MD. 199 pp. New York, Praeger Publishers, Inc, 1986. $38.95 (hardcover)

The Last Taboo. Money as Symbol and Reality in Psychotherapy and Psychoanalysis. By David W. Krueger, MD. 262 pp, illustrated. New York, Brunner/Mazel, 1986. $27.50 (hardcover)

RADIOLOGY

Angiographic Diagnosis of Supratentorial Cerebral Tumours. (Compared with CT Scan). By A. Pansini and P. Conti, 280 pp, illustrated. St. Louis, Mo, Ishiyaku EuroAmerica, Inc, 1985. $80.00 (hardcover)

Radiology of Adverse Reactions to Drugs and Toxic Hazards. By George Ansell, MD. 389 pp, illustrated. Rockville, Md, Aspen Publications, 1985. $40.00 (hardcover)

SURGERY

Atlas of Stapling Techniques. By Pedro A. Rubio, MD. 368 pp, illustrated. Rockville, Md, Aspen Publishers, Inc, 1986. $95.00 (hardcover)

Medical Assessment of the Elderly Surgical Patient. By Gwyn Seymour, MB. 315 pp, illustrated. Rockville, Md, Aspen Systems Corp, 1986. $37.50 (hardcover)

TOXICOLOGY

Basic Toxicology. Fundamentals, Target Organs, and Risk Assessment. By Frank C. Lu. 276 pp, illustrated. New York, Hemisphere Publishing Corp, 1985. $49.95 (hardcover)

OBITUARIES

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Stuart C. Alexander, MD, New York. Died February 24, 1986; age 61. Dr Alexander was a 1949 graduate of Johns Hopkins University School of Medicine, Baltimore. He was a Fellow of the American College of Chest Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the American Thoracic Society, the New York County Medical Society, and the Medical Society of the State of New York.

Harry Seymour Altman, MD, Bronx. Died December 12, 1985; age 86. Dr Altman was a 1921 graduate of New York University College of Medicine, New York. He was a Diplomate of the American Board of Pediatrics and a member of the Academy of Medicine, the American Academy of Pediatrics, the Bronx County Medical Society, and the Medical Society of the State of New York.

Morris A. Altman, MD, Suffern. Died April 16, 1986; age 82. Dr Altman was a 1929 graduate of State University of New York Downstate Medical Center, New York. He was a Fellow of the American College of Angiology and a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Joseph Berte, MD, Brooklyn. Died May 18, 1986; age 96. Dr Berte was a 1928 graduate of Eclectic Medical College, Cincinnati. He was a Fellow of the American Academy of Family Practice and a member of the New York Cardiological Society, the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Philip Brody, MD, Brooklyn. Died April 28, 1986; age 87. Dr Brody was a 1923 graduate of New York University College of Medicine, New York. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Samuel C. Burchell, MD, New York. Died April 24, 1986; age 89. Dr Burchell was a 1921 graduate of Columbia University College of Physicians and Surgeons, New York. He was a Diplomate of the American Board of Psychiatry and Neurology and a member of the New York Neurological Society, the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

Theodore F. Ciesla, MD, Amherst. Died April 17, 1986; age 83. Dr Ciesla was a 1931 graduate of the University of Buffalo School of Medicine. He was a Fellow of the American College of Chest Physicians and a member of the American Thoracic Society, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Howard Andrew English, MD, Warnerville. Died May 2, 1986; age 76. Dr English was a 1937 graduate of the State University of New York Downstate Medical Center, New York. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Andrew Fellini, MD, Bronx. Died March 7, 1986; age 58. Dr Fellini was a 1959 graduate of Universita Degli Studi di Bologna, Facolta di Medicina e Chirurgia. He was a Fellow of the American College of Anesthesiologists and the American College of Chest Physicians, and a Diplomate of the American Board of Anesthesiology. His memberships included the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Bronx County Medical Society, and the Medical Society of the State of New York.

Leonard Goldfarb, MD, Syracuse. Died March 29, 1986; age 57. Dr Goldfarb was a 1963 graduate of Universite de Paris Faculte de Medecine. He was a member of the American Psychiatric Association, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Frank Peter Guidotti, MD, New York. Died May 27, 1986; age 78. Dr Guidotti was a 1933 graduate of Universita di Napoli Facolta di Medicina e Chirurgia. His memberships included the Academy of Medicine, New York State Society of Occupational Medicine, American Occupational Medical Association, American Public Health Association, Pan American Medical Association, the New York County Medical Society, and the Medical Society of the State of New York.

George Richard Kinsella, MD, Oneida. Died May 11, 1986; age 62. Dr Kinsella was a 1955 graduate of State University of New York Upstate Medical Center, Syracuse. He was a member of the Academy of Medicine, the Medical Society of the County of Madison and the Medical Society of the State of New York.

Solomon Israel Kuper, MD, Binghamton. Died May 20, 1986; age 63. Dr Kuper was a 1948 graduate of the University of the Witwatersrand Medical School, Johannesburg. He was a Fellow of the American College of Surgeons and a member of the Broome County Medical Society and the Medical Society of the State of New York.

Vito La Rocca, MD, Bronx. Died March 2, 1986; age 82. Dr La Rocca was a 1928 graduate of Universita Degli Studi di Palermo, Facolta di Medicina e Chirurgia. He was a Diplomate of the American Board of Ophthalmology and a member of the New York County Medical Society and the Medical Society of the State of New York.

Louis Leiter, MD, Bronx. Died May 5, 1986; age 88. Dr Leiter was a 1922 graduate of Rush Medical College, Chicago. He was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Recka Mandelbaum, MD, New York. Died January 13, 1986; age 91. Dr Mandelbaum was a 1920 graduate of

Julius-Maximilians-Universitat Fakultat, Wurzberg, Bavaria. Dr Mandelbaum was a member of the New York County Medical Society and the Medical Society of the State of New York.

Max Maron, MD, Allentown, Pennsylvania. Died January 22, 1986; age 77. Dr Maron was a 1936 graduate of Hamburgische Universitat Medizinische Fakultat, Hamburg. He was a Fellow of the American Academy of Family Practice and a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

John William Mills, MD, Horseheads. Died May 10, 1986; age 57. Dr Mills was a 1955 graduate of the State University of New York Upstate Medical Center, Syracuse. Dr Mills was a Fellow of the American Academy of Family Practice, a Diplomate of the American Board of Family Practice, and a member of the Medical Society of the County of Chemung and the Medical Society of the State of New York.

Fernando Moreno-Pagan, MD, New York. Died May 15, 1986; age 65. Dr Moreno-Pagan was a 1950 graduate of Laval University Faculty of Medicine, Quebec. He was a Fellow of the American College of Allergists and a Diplomate of the American Board of Pediatrics. His memberships included the American Academy of Pediatrics, the American Academy of Allergy, the New York County Medical Society, and the Medical Society of the State of New York.

John Richard Murphy, MD, Saranac Lake. Died May 5, 1986; age 82. Dr Murphy was a 1935 graduate of State University of New York Upstate Medical Center, Syracuse. He was a member of the Medical Society of the County of Franklin and the Medical Society of the State of New York.

Paula Nojarova, MD, New York. Died May 17, 1986; age 72. Dr Nojarova was a 1941 graduate of Zagrebaskog Universiteta Medecinski Fakultet, Zagreb. Dr Nojarova was a member of the New York County Medical Society and the Medical Society of the State of New York.

Tibor Andrew Nyilas, MD, Elmhurst. Died May 19, 1986; age 72. Dr Nyilas was a 1937 graduate of Eotvos Lorand Tudomanyegyetem Orvostudomanyi Fakultas, Budapest. Dr Nyilas was a member of the American Academy of Family Practice, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Gilbert M. Palen, MD, Margaretville. Died May 17, 1986; age 73. Dr Palen was a 1939 graduate of Duke University School of Medicine, Durham. He was a Qualified Fellow of the International College of Surgeons and a member of the Delaware County Medical Society and the Medical Society of the State of New York.

Abraham Rosenthal, MD, Kew Gardens. Died May 15, 1986: age 75. Dr Rosenthal was a 1934 graduate of New York Medical College, Flower and Fifth Avenue Hospitals, New York. He was a Fellow of the American College of Surgeons and a member of the Academy of Medicine, the New York Pathological Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Frank Schwimmer, MD, New York. Died March 7, 1986; age 81. Dr Schwimmer was a 1930 graduate of the University of Kansas School of Medicine, Lawrence-Kansas City. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Victor Royce Syracuse, MD, Glendale, California. Died May 5, 1986, age 91. Dr Syracuse was a 1923 graduate of Jefferson Medical College of Philadelphia. He was a Qualified Fellow of the International College of Surgeons and a Diplomate of the American Board of Ophthalmology and the American Board of Otolaryngology. His memberships included the New York Society for Clinical Ophthalmology, the American Academy of Ophthalmology and Otolaryngology, the American Society of Plastic and Reconstructive Surgery, the New York County Medical Society, and the Medical Society of the State of New York.

Henry Tanner, MD, Boca Raton, Florida. Died March 31, 1986; age 82. Dr Tanner was a 1930 graduate of Tulane University School of Medicine, New Orleans. He was a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Irwin Paul Train, MD, Forest Hills. Died February 22, 1986; age 81. Dr Train was a 1930 graduate of New York Medical College, Flower and Fifth Avenue Hospitals, New York. He was a Fellow of the American College of Surgeons and the American College of Gastroenterology, and a Diplomate of the American Board of Surgery. His memberships included the New York County Medical Society and the Medical Society of the State of New York.

Sidi B. Wasser, MD, Merrick. Died May 12, 1986; age 73. Dr Wasser was a 1940 graduate of Universitatea din Bucuresti Facultatea de Medicina. Dr Wasser was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Nassau County Medical Society, and the Medical Society of the State of New York.

David M. Weinstock, MD, Forest Hills. Died May 5, 1986; age 75. Dr Weinstock was a 1939 graduate of Universite de Lausanne Faculte de Medecine. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Gonsalvo C. Williams, MD, Dobbs Ferry. Died April 26, 1986; age 90. Dr Williams was a 1925 graduate of Yale University School of Medicine, New Haven. He was a member of the Medical Society of the County of Westchester and the Medical Society of the State of New York.

Berthold Zoffer, MD, New York. Died May 4, 1986; age 70. Dr Zoffer was a 1943 graduate of Middlesex University School of Medicine, Waltham. Dr Zoffer was a Fellow of the American College of Anesthesiologists and a member of the Academy of Medicine, the New York State Society of Anesthesiologists, Inc, the Academy of Psychosomatic Medicine, the American Geriatrics Society, the American Society of Clinical Hypnosis, the New York County Medical Society, and the Medical Society of the State of New York.

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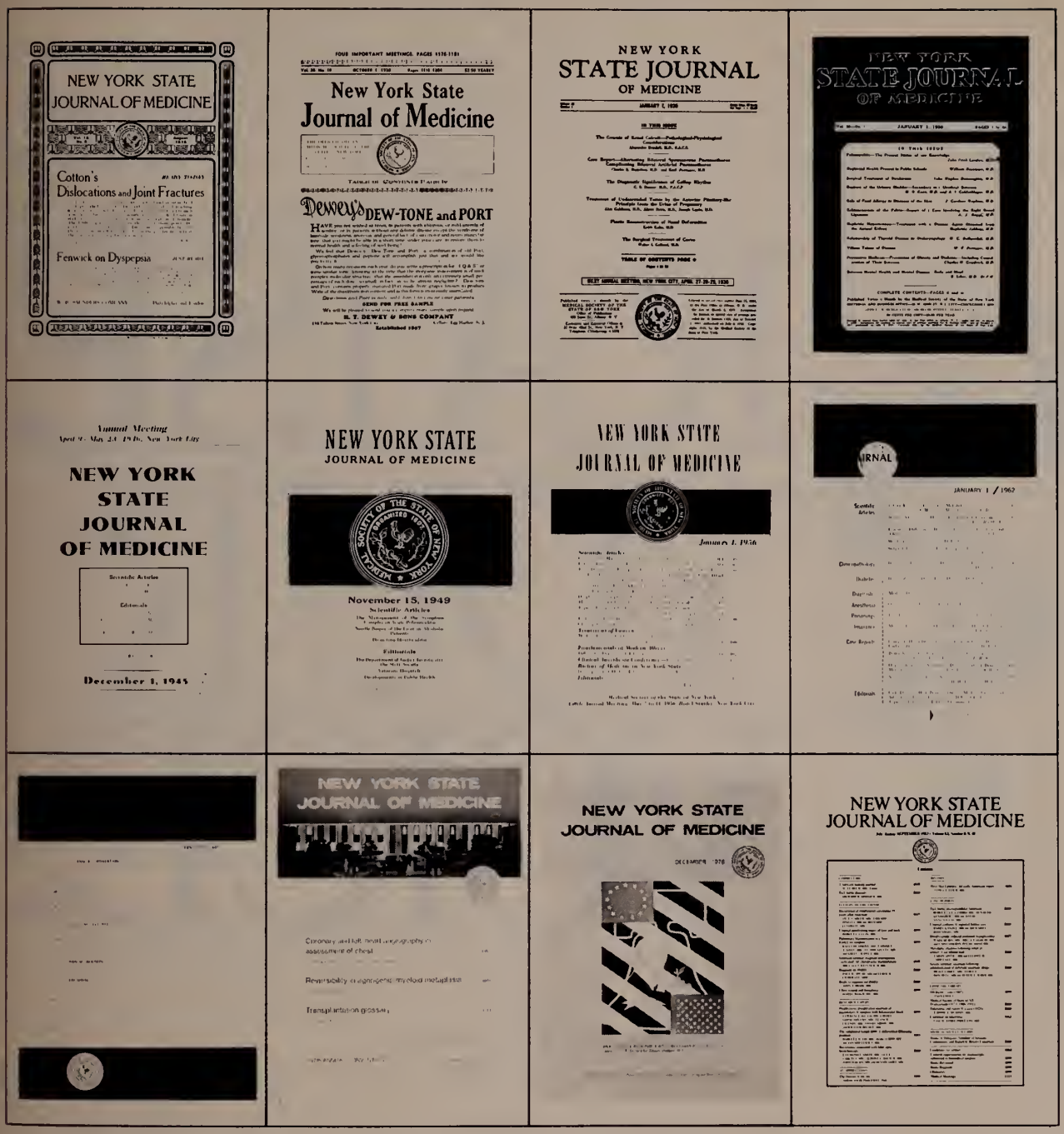

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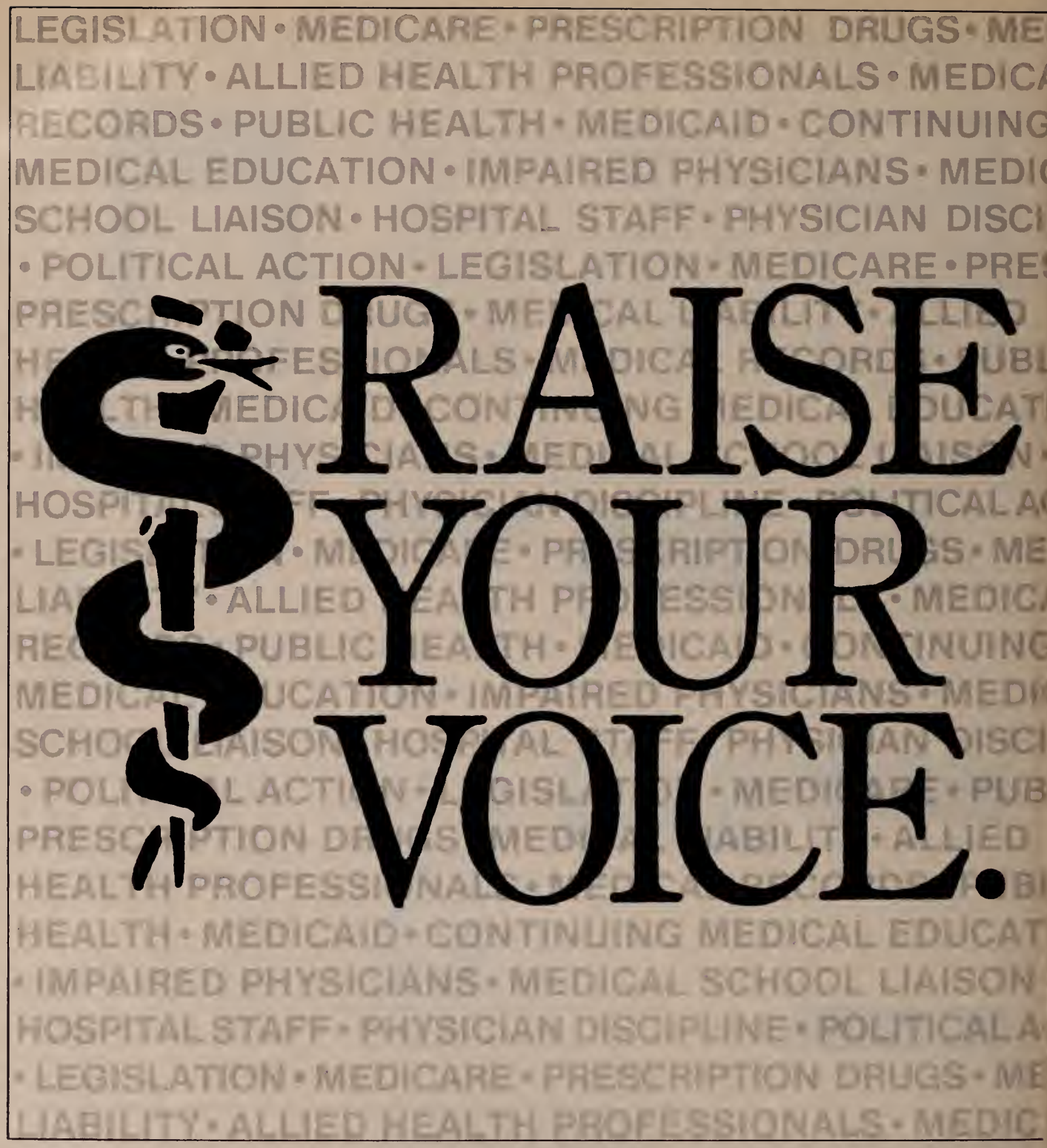

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Oct 26–31. **17th Family Medicine Review.** 50 Cat 1 Credits. Hyatt Regency Hotel, Lexington. Info: University of Kentucky College of Medicine, Office of Continuing Education, 132 COM Office Building, Lexington, KY 40536-0086. Tel: (606) 233-5161.

LOUISIANA

Oct 6–10. **12th Annual Meeting of the American Association of Pathologists' Assistants.** Le Pavillion Hotel, New Orleans. Info: Ms Anne Walsh Feeks, Department of Pathology, New York University Medical Center, 550 First Ave, New York, NY 10016. Tel: (212) 340-5747.

Oct 17–19. **Assessment of Arteries and Veins by Duplex Ultrasound.** 18 Cat 1 Credits. New Orleans. Info: Lisa Krehbiel, Institute for Medical Studies, 30131 Town Center Dr, Suite 215, Laguna Niguel, CA 92677. Tel: (714) 495-4499.

Oct 18. **The Basics of Office Based Surgery.** New Orleans Marriott. Info: Betty D. Watts, Administrative Assistant, American Society of Outpatient Surgeons, PO Box 33185, San Diego, CA 92103. Tel: (619) 692-9918.

MARYLAND

Oct 6–8. **Platelet Transfusion Therapy.** 13 Cat 1 Credits. Masur Auditorium, Warren Grant Magnuson, Clinical Center, Bethesda. Info: Sharon Feldman, Prospect Associates, 1801 Rockville Pike, Suite 500, Rockville, MD 20852. Tel: (301) 468-6555.

Oct 9–11. **12th Annual Topics in Gastroenterology and Liver Disease.** 20½ Cat 1 Credits. The Johns Hopkins Medical Institutions, Baltimore. Info: Jeanne Ryan, Program Coordinator, Office of Continuing Education, The Johns Hopkins University School of Medicine, 720 Rutland Ave, Baltimore, MD 21205. Tel: (301) 955-5880.

MASSACHUSETTS

Oct 31–Nov 1. **Annual Meeting, New England Chapter, American College of Sports Medicine.** Sheraton Inn, Boxborough. Info: Sharon Peachy, Boston University, 36 Cummington St, Boston, MA 02215. Tel: (617) 353-2717.

SOUTH CAROLINA

Oct 6–10. **The 1986 Physician in Management Series I and II.** 31 CME Credits. The Omni Charleston Place, Charleston. Info: Sherry Mason, American Academy of Medical Directors, 4830 W Kennedy Blvd, Suite 648, Tampa, FL 33609. Tel: (813) 873-2000.

AROUND THE WORLD

SHANGHAI, PEOPLE'S REPUBLIC OF CHINA

Oct 25–31. **First International Respiratory Failure Conference.** 24 hours CME Credit. Info: First International Respiratory Failure Conference, People to People Citizen Ambassador Program, Dwight D. Eisenhower Building, Spokane, WA 99202. Tel: (509) 534-0430.

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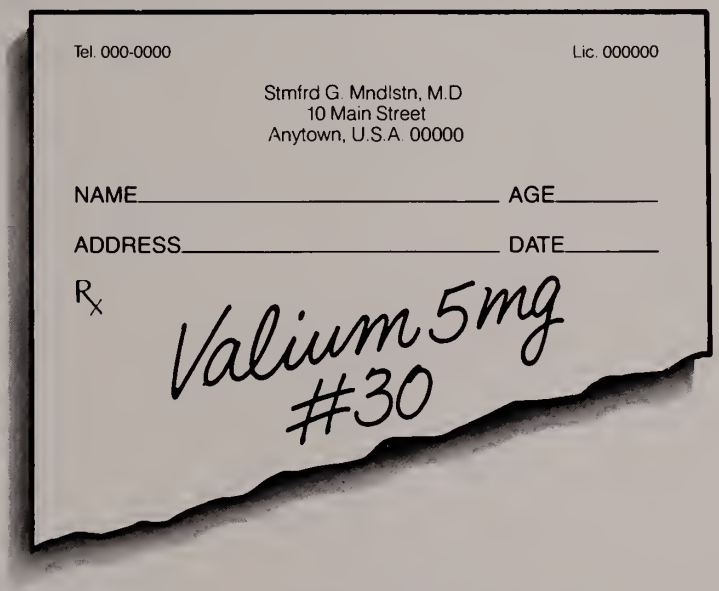

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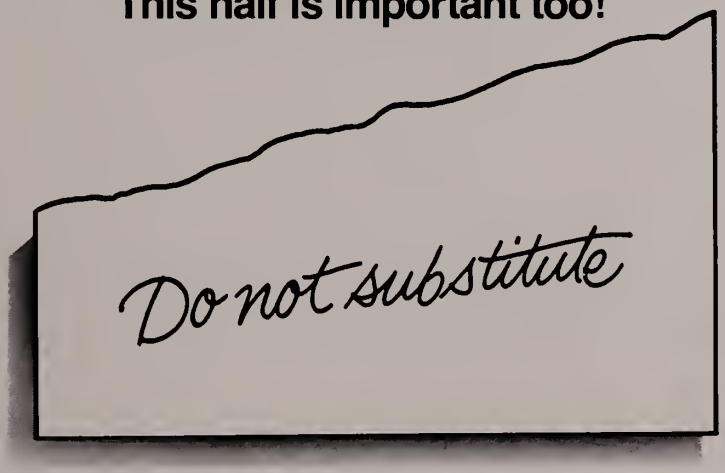

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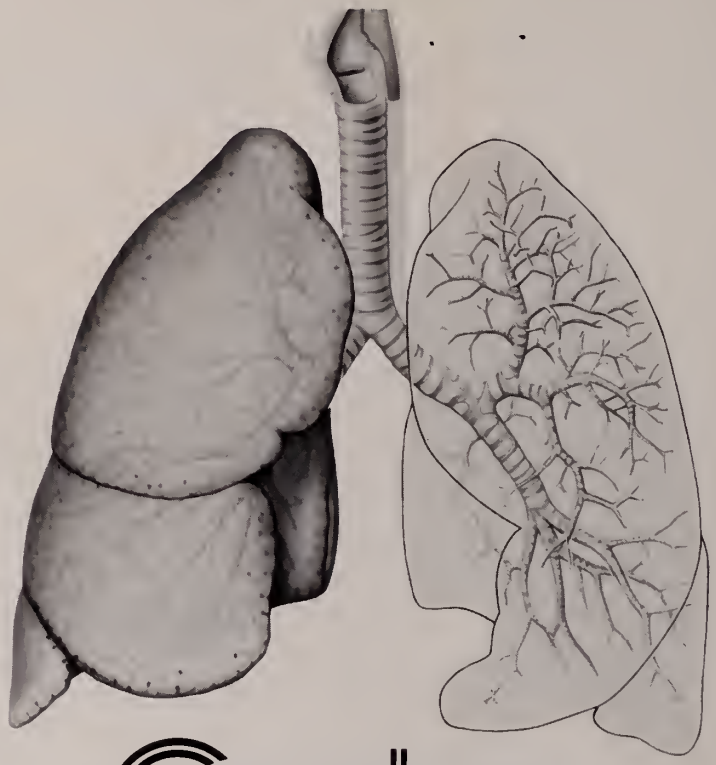

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Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- In renal impairment, safe dosage of Ceclor may be lower than that usually recommended. Ceclor should be administered with caution in such patients.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, erythema multiforme, serum-sickness-like reactions): 1.5%; usually subside within a few days after cessation of therapy. These reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children)
- Abnormal urinalysis; elevations in BUN or serum creatinine
- Positive direct Coombs' test
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly)

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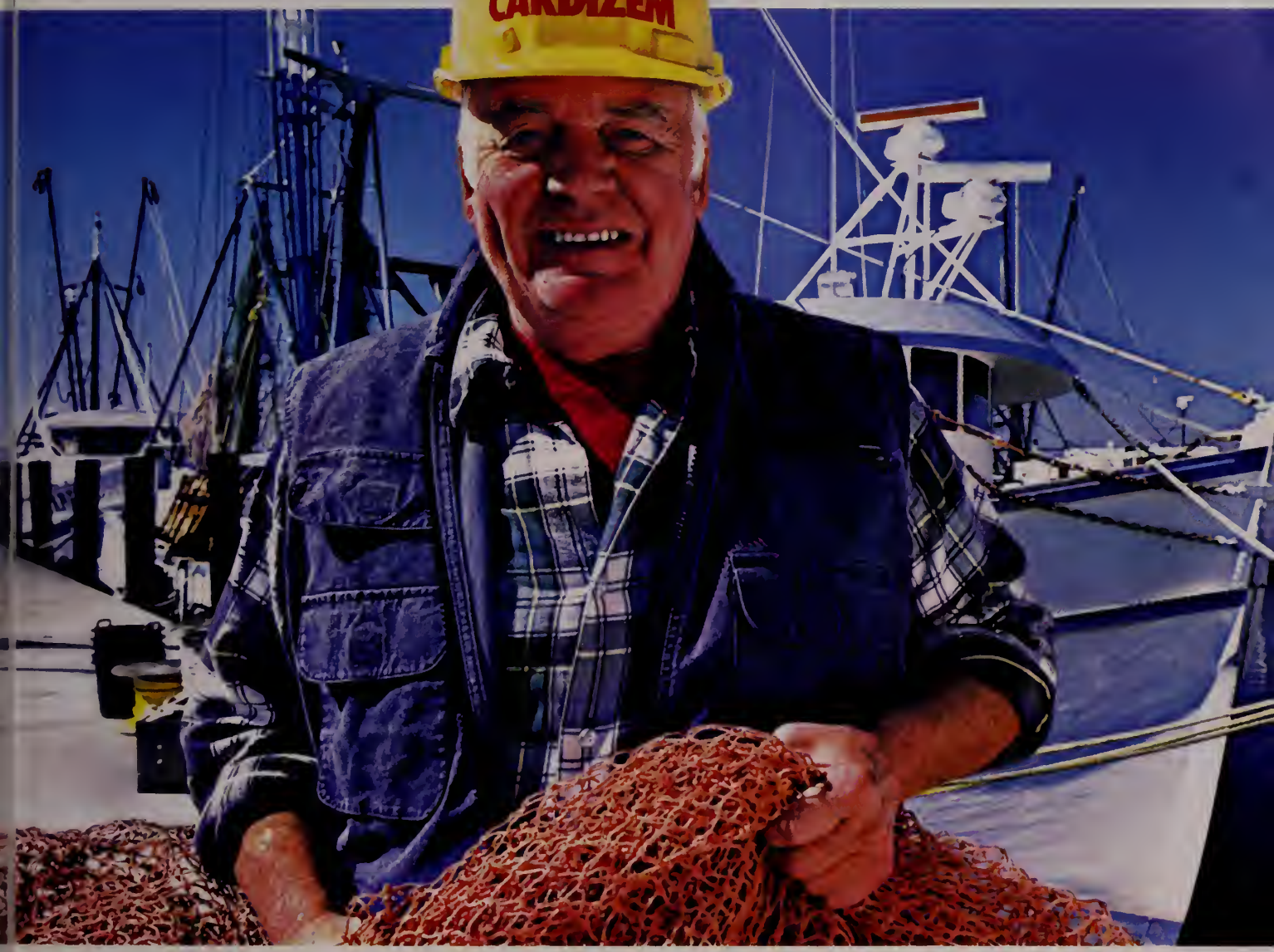

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- ***Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate***
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***See Warnings and Precautions.**

Please see brief summary of prescribing information on the next page.

CARDIZEM® FEW SIDE EFFECTS IN ANTIANGINAL THERAPY

diltiazem HCl/Marion

60 mg tid or qid

Brief Summary
Professional Use Information

CARDIZEM®
(diltiazem HCl) 30 mg and 60 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor
Gastrointestinal	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. Issued 7/86

See complete Professional Use Information before prescribing.

References: 1. Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers. Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983, 106(6) 1341-1347 **2.** Shapira W: Calcium channel blockers. Actions on the heart and uses in ischemic heart disease. Consultant 1984, 24(Dec) 150-159 **3.** Johnston DL, Lesowoy R, Humen DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985, 55 680-687 **4.** Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39 **5.** Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982, 50(Sept) 94-116

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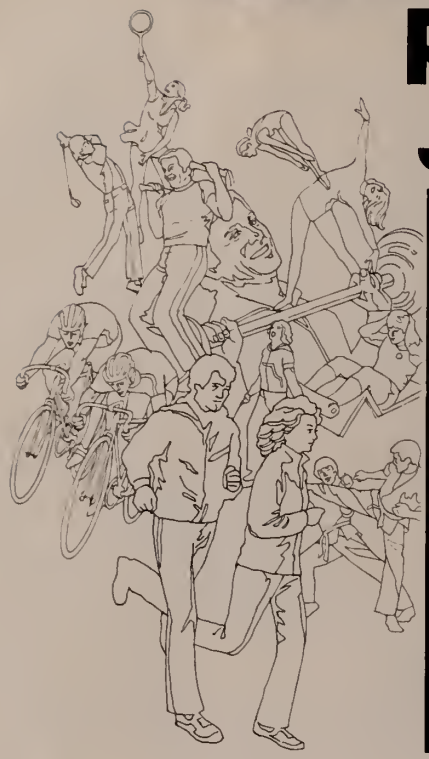

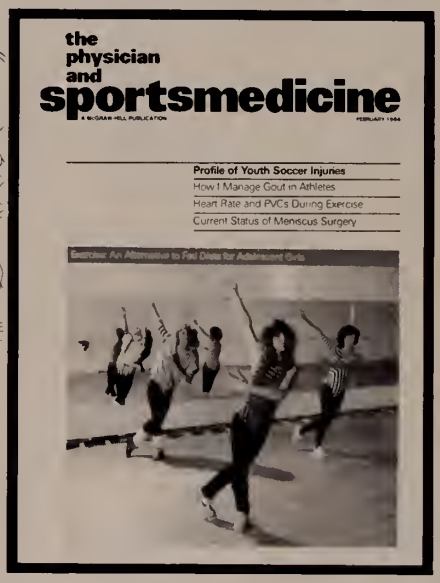

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Nov 12–14. **Chemotherapy Foundation Symposium VII, Innovative Cancer Chemotherapy for Tomorrow.** Sheraton Centre Hotel. Info: Director, Page and William Black Post-Graduate School of Medicine, One Gustave L. Levy Place, New York, NY 10029. Tel: (212) 650-6772.

Nov 19. **The New Economics of Medical Care: The Identifier Concept.** 6 Cat 1 Credits. The Warwick Hotel. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Nov 19–20. **The First Conference on DNA Topoisomerases in Cancer Chemotherapy.** 12 1/2 Cat 1 Credits. Info: NYU Medical Center, Post-Graduate Medical School, Registration Department, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Nov 22. **Penile Prostheses in the Treatment of Erectile Dysfunction.** Podell Auditorium, Beth Israel Medical Center. Info: Beverley R. Baptiste, Medical Education Office, Beth Israel Medical Center, First Ave, at 16th St, New York, NY 10003.

Nov 22. **The Clinician and the Treatment of Schizophrenia: The Newer Options.** Roosevelt Hotel. Info: Lester E. Shapiro, MD, New York Psychiatric Association, Inc, 420 E 76 St, New York, NY 10021. Tel: (516) 766-3442.

Nov 19–22. **Controversial Issues in Rhinoplasty.** 18 Cat 1 Credits. The Waldorf-Astoria Hotel. Info: Francine Leinhardt, Coordinator, Manhattan Eye, Ear and Throat Hospital, 210 East 64 St, New York, NY 10021. Tel: (212) 838-9200, Ext 2776.

NASSAU

Nov 5. **Infections in the Elderly.** 6 Cat 1 Credits. Jewish Institute for Geriatric Care, New Hyde Park. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Nov 14. **Dementia in the Elderly Years.** 4 Cat 1 Credits. Rust Auditorium, North Shore University Hospital. Info:

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(*continued on p 12A*)

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9:00 a.m. - 1:00 p.m. General Session: Clinical and Ethical Dilemmas, *Gramercy A & B*

2:00 p.m. - 5:00 p.m.
Chest Diseases, *Regent Parlor*
Cardiovascular Diseases, *Murray Hill B*
Pediatrics/Orthopedic Surgery, *Murray Hill A*
Neurology/Alcoholism, *Nassau A*
Emergency Medicine/Critical Care/Otolaryngology, *Gramercy B*
Medical Liability, *Gramercy A*

SATURDAY, MARCH 14

10:00 a.m. - 1:00 p.m.
Internal Medicine (All Day), *Regent Parlor*
Ophthalmology (All Day), *Sutton Parlor Center*
Psychiatry (All Day), *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation (All Day), *Murray Hill A*
Urology/Pathology, *Nassau A*
Dermatology, *Nassau B*

2:00 p.m. - 5:00 p.m.
Internal Medicine, *Regent Parlor*
Ophthalmology, *Sutton Parlor Center*
Psychiatry, *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation, *Murray Hill A*
Computers in Medicine, *Madison Suite*
Terrorism in Medicine, *Sutton Parlor South*

SUNDAY, MARCH 15

10:00 a.m. - 1:00 p.m.
Allergy and Immunology, *Murray Hill B*
General Surgery/Radiology/Anesthesiology, *Murray Hill A*
Obstetrics and Gynecology/Women's Medical Society of New York State, *Gramercy B*
Family Practice/Orthopedic Surgery, *Nassau A*
Neurosurgery, *Morgan Suite*

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NEW YORK STATE
JOURNAL OF MEDICINE

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COMMENTARIES

Medical malpractice and foreign medical graduates

Multivariate analysis applied to correlating the loci of undergraduate medical education with rates of medical malpractice is extremely difficult because of the inaccessibility of much of the required information. There are a number of confounding variables about which precise information must be obtained. These include the volume of patients seen, the physician's specialty, the seriousness of the condition treated, and the profile of patients in the physician's practice, to name a few. If this information could be gotten, then multivariate analysis might produce valid results. The lure of making single variable comparisons without controlling for confounding factors is great, but leads to invalid results.

A recent study published in the *FMG Newsletter* attempts to correlate medical malpractice rates in New York State's Queens County according to single variables.[1] This study, conducted by the Committee for Fairness and Equality in Medicine, concludes that graduates of US medical schools are sued twice as often as those of certain other countries.[1] The 563 medical malpractice lawsuits brought in Queens County during 1982–1984 were examined and the defendant physicians' names researched in the *American Medical Directory*.[2] Data were collected on location of medical school, sex, year of licensure, and medical specialty. It was found that while foreign medical school graduates (FMGs) made up 62% of the area's physicians, they accounted for only 56% of the physicians sued. Some 13% of FMGs had been sued compared to 29% of US medical school graduates (USMGs). Comparisons were then made according to the states and countries in which USMGs and FMGs attended medical school. According to this study, 50% of the graduates of schools from Virginia were sued, 45% of those from Kentucky, 43% of those from Louisiana, and 28% of those from New York. The worst overseas records were among those from schools in Scotland (32%), Belgium (31%), Israel (28%), and Iran (26%). The best records were among those from schools in the USSR (2%), Poland (2%), Romania (7%), Haiti (7%), and Mexico (8%). The authors made a point of saying that few countries performed as poorly as the leading state suppliers of physicians.

Malpractice suit rates were also examined by school. The Middlesex University (now defunct) had the highest rate (46%), followed by Chicago Medical School (42%), the Faculty of Medicine of the University of Geneva (36%), and SUNY Health Science Center at Buffalo (32%). Rates were also examined by specialty, and again USMGs were found to be sued more often than FMGs in the specialties with the highest rates of litigation: obstetrics and gynecology, neurology, otolaryngology, radiology, anesthesiology, general surgery, and urology.

The authors of this study conclude that "USMGs are much more likely to be sued than are FMGs, that wide variations exist among graduates from various states and foreign countries, and that the medical community has not been successful in inculcating uniformity into U.S. medical school training."[1]

The authors of this study have obviously set out to demonstrate that USMGs are not as well trained as FMGs, using rates of malpractice suits as a measure of the quality of undergraduate medical training. Their study fails to convince because it is so seriously flawed in both design and analyses as to make its conclusions meaningless.

The authors assert that the characteristics of Queens County parallel those of other urban areas. The facts speak to the contrary. Queens currently has large populations of recent immigrants—Greeks, Chinese, Koreans, and Indians, to name a few—and many illegal aliens. These groups are less likely than citizens to sue physicians, but are frequently served by FMGs. This reality alone would, if factored in as a control in an appropriately designed study, produce vastly different results.

The data are based on the number of suits brought and not the number that were successful. Thus the rates are reflective of patient population characteristics, including tendencies to sue, and not physician competence, which might be reflected in the number of cases lost and won by physicians.

The use of the *American Medical Directory*, which lists physicians by address, poses a problem.[2] FMGs with listed home addresses in Queens may work in institutions outside of the borough, such as in Manhattan. Including

them in the denominator lowers the percentage of FMGs sued. The authors, while acknowledging this source of bias, dismiss it as being of little significance, which it is not.

It is possible to determine from the *American Medical Directory* whether or not a physician is involved in direct patient care. This is a very important variable in estimating the percentage of physicians sued for medical malpractice. Yet this was not done.

Those familiar with medical malpractice are aware that it is a function of many variables that are not included in this study. These include: size of practice, socio-economic-educational status of patients, difficulty and seriousness of medical problems, type of practice (eg, fee for service, HMO, part-time employment), and years in practice. By ignoring these critical variables the authors have produced a seriously defective study and incorrect results. This approach, if similarly applied to hospitals, would result in the conclusion that small proprietary hospitals offer better medical care than university and tertiary care ones. The higher mortality rates observed in the latter two are reflective of the complicated, high risk nature of the cases handled in these institutions, not physician incompetence.

The analyses by state, country, and institution are meaningless without taking into consideration the variables mentioned above. This deficiency is underscored by the fact that, according to the authors, the graduates of the most prestigious medical schools have the highest rates of malpractice suits.

The authors state that an average of 1.4 physicians were named in each suit. Physicians who are supervisors or directors of service are often named in suits concerning patients for whom they did not provide any direct care. Failure to control for this leads to incorrect conclusions.

The authors state that "The issue of physician competence is a complicated one and this study helps to reaffirm that fact." What their study does reaffirm is that a complex issue such as this cannot be addressed as they have done, namely, by simple numerator/denominator comparisons of medical malpractice rates in a unique county in the United States. Such comparisons, carried out even in the best of statistically designed studies, would still have to contend with the influence of postgraduate training in the United States on both FMG and USMG competence. A number of studies among Fifth Pathway students, for example, have demonstrated that, at least for these academically selected Americans from foreign medical schools, professional performance measures up to that of US-trained peers.[3,4] The clinical performance of Americans accepted into the third year of an American medical school after two years in a foreign one has also been evaluated. These carefully selected students perform as well clinically as those enrolled from the first year.[5] Benson et al[6] have looked into the performance of USFMGs on certifying examinations in internal medicine. They found that among first-time takers in 1980, 82% of USMGs passed, 45% of alien FMGs, and 38% of USFMGs. All of the variables inherent in the findings of studies such as these would have to be taken into consideration in the design of any research protocol that attempted to compare medical malpractice rates by site of undergraduate medical education.

Foreign medical graduates contribute much to American medicine in the areas of patient care, research, and teaching. They are an integral part of the American medical care system. Their interests are ill served by statistically invalid studies that unconvincingly attempt to demonstrate that their undergraduate medical training in and of itself makes them less likely to be sued for medical malpractice than their American-trained colleagues.

PASCAL JAMES IMPERATO, MD
Editor

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Adult respiratory distress syndrome

Adult respiratory distress syndrome (ARDS) (or increased permeability pulmonary edema) was defined by Petty and Ashbaugh[1] in 1971. It is a disturbance of body homeostasis characterized by severe hypoxemia unresponsive to increasing concentrations of oxygen (most likely due to intrapulmonary right-to-left shunting via fluid-filled and atelectatic alveoli), bilateral diffuse infiltrates on chest roentgenogram, and an increase in lung stiffness. ARDS occurs in adults and is usually associated with a normal pulmonary capillary wedge pressure (PCWP). The clinical disorders associated with this problem are legion and include sepsis, shock, trauma, aspiration, drugs, inhaled toxins, and metabolic disorders, to list but a few.

Despite extensive research involving animals as well as humans, the introduction of modern, expensive, mechanical ventilators that can deliver almost any combination of respiratory gases in almost any conceivable manner, and nearly 20 years of experience with the problem, the mortality rate for this abnormal state remains approximately 60%.[2]

Many studies have been performed in an attempt to predict both the development of ARDS as well as its outcome. Fowler et al[3] studied 88 patients with ARDS and concluded that there were four variables that were significantly associated with poor survival when independently examined. These were: fewer than ten band forms on the white blood cell differential count, an arterial pH of less than 7.4, a calculated bicarbonate level of less than 20 mEq/L, and the presence of uremia. Bell et al[4] put forth the view that both infection and multiple organ involvement are closely associated with mortality. Montgomery et al[5] reported that in 207 patients with ARDS, early mortality (within 72 hours of entry into the study) was due to the original presenting illness or injury, whereas late mortality (more than 72 hours after entry into the study) was most often due to sepsis. Cardiac failure as well as multiorgan failure were also causative factors, but were not seen as often as sepsis. A multitude of mediators and markers, eg, factor VIII antigen[6] and phospholipase A_2,[7] have been proposed for selecting out those patients who are most at risk of developing and of dying of ARDS. None of these indicators, however, has passed the test of time.

Wherein lies the problem in this syndrome? First, if one looks at the Starling Equation of net fluid exchange (Q_F), one finds that

$$Q_F = K\,(P_c - P_{IS}) - \sigma\,(\Pi_{PI} - \Pi_{IS})$$

where K is the membrane filtration coefficient, P_c and P_{IS} represent the capillary and interstitial fluid hydrostatic pressure, σ is the reflection coefficient, and Π_{PI} and Π_{IS} represent the plasma and interstitial fluid oncotic pressure.[8] Since P_c, P_{IS}, and σ cannot be measured directly and since this Starling Equation represents the physiological factors involved in net fluid exchange, we lack those fundamental values that are needed to understand flow across the capillary, interstitial, and alveolar spaces. This deficit puts us at a physiological disadvantage.

If one examines all the disease states that make up ARDS, the various ages of those with the syndrome, the presence or lack of underlying serious disease prior to the development of ARDS, and the lack of uniformity in definition as well as reporting of this abnormality, it is not difficult to see that we are often at a clinical disadvantage.

The present therapy for ARDS, including positive end-expiratory pressure (PEEP), mechanical ventilation, O_2, etc, in effect merely constitutes prophylactic measures and supportive care for patients during the critical period of illness until host recovery occurs. The lack of more specific therapy puts us at a management disadvantage.

Finally, at the present time we are unable to pinpoint the exact mechanism of the onset of ARDS. Hence, we are at an etiological disadvantage.

When looked at from the above perspective, and when one reviews all these impediments and shortcomings in our knowledge of ARDS, it is little wonder that the mortality rate associated with this syndrome is so high.

In this issue of the *Journal*, Brandstetter et al[9] present five adolescent patients, all of whom had ARDS secondary to gastric aspiration, and all of whom survived. In view of the mortality statistics presented above, this accomplishment is to be lauded. One might quibble and say these patients were all very young, none had underlying disease, multisystem organ failure was not present, severe infection did not ensue, and all were quickly treated. How true these words are. Indeed, these are the probable reasons why these ARDS patients survived, but survive they did.

The hope at present is to find a common thread of causality which will bind together the sundry maladies encompassed by the term ARDS. Up until now many theories have been put forward. These include activation of the complement system, release of superoxide ions,[10] leukocyte degranulation, prostaglandin abnormalities, etc.[11] Most recent investigations have been directed toward mediation of ARDS by leukocytes.[12] Cell-cell interactions between leukocytes and endothelial cells have been proposed by recent researchers.[13] Unfortunately, none of these mechanisms can be demonstrated to be present in all the diseases that lead to ARDS.

It is readily apparent that increased alveolo-capillary membrane permeability exemplifies one particular final common pathway in lung injury. Perhaps our problem as investigators in the field of ARDS is that we have not dug deeply enough into the molecular biology of the problem. Most physicians can recite a litany of causes of ARDS and many scientists can point out each theory of origin, but very few have carefully examined the molecular structure of the alveolo-capillary membrane with regard to its biochemistry or its elemental structure from a submicroscopic point of view. It is probably at this level that the abnormality exists and it is at this level that one must look. The work of Brigham and his associates at Vanderbilt comes closest to this method.[14,15] The work of Demling[16] and his associates in California on the effects of prostaglandins on pulmonary microvascular injury are also interesting and should prove helpful. Hopefully the work of others will continue so that the fundamental alveolo-capillary membrane changes can be discovered and so that within the near future the mysteries of ARDS will be solved. Once this occurs, specific treatment can be directed at the precise pathophysiological abnormality. This should then improve our present 40% survival rate for patients with ARDS.

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Endourology

Endourology has evolved in the past decade as a sophisticated method for treating urologic diseases in a manner that obviates the need for open surgery in a large number of patients. In the broadest sense the term endourology refers to any endoscopic procedure or examination performed anywhere in the urinary tract from the urethra to the kidney. However, during the past several years the term has come to refer to any procedure performed through a percutaneous approach to the kidney and upper collecting system and also to retrograde ureteroscopy. Physicians need to keep abreast of these new developments so that patients are offered the most effective and least invasive form of therapy in the management of stone disease.

The combined approach to the urinary tract by both urologists and radiologists has opened new pathways for treating pathology in either the upper or lower urinary tract. Similar advances in the history of medicine have rarely occurred so rapidly. Two articles, by Gordon et al[1] and Cubelli and Smith,[2] presented in this issue of the *Journal*, complement each other. These papers are much needed since the science of endourology is new and relatively few reports have been written as yet. Gordon et al[1] thoroughly summarize the origins of the subspecialty. This began with percutaneous renal puncture, antegrade installation of contrast material, and percutaneous drainage (nephrostomy), which occurred in the early 1950s. Using smaller portals of access to the renal pelvis and ureter than had been provided with the surgical blade, the percutaneous method has been expanded to include the drainage of retroperitoneal abscesses and the alleviation of ureteral-pelvic junction obstructions. In addition, the concomitant use of the ureteroscope and special baskets, forceps, and ultrasonic sonotrodes have allowed for the extension of many standard cystoscopic techniques to the entire upper urinary tract. The culmination of this technical revolution has recently been seen with the introduction of extracorporeal shock wave lithotripsy (ESWL). The use of focused high energy shock waves has allowed the surgeon to disintegrate calculi in a virtually noninvasive manner. Through a combined approach using percutaneous methods, ureteroscopy, and ESWL, open surgery has been avoided in as many as 90–95% of patients with stone disease in institutions where expertise is available.

Successful percutaneous removal of urinary tract calculi can be expected in from 70% to 95% of patients who are appropriately selected.[3,4] After the creation of a percutaneous tract, removal of stones can be performed either by basket extraction or, in the case of larger stones, by ultrasonic lithotripsy and fragmentation. Cubelli and Smith report that 97% of their patients were stone free following the extraction of smaller calculi. Eighty-six percent of those with staghorn stones were also rendered stone free.[2] These are excellent results. The hope of the surgeon is that stone recurrence rates will be lower with these new modalities than following open surgery and that no significant changes in renal function will occur. Long term follow-up of this and other procedures will be interesting. There is little question, however, that the success rate of percutaneous removal of calculi compares favorably with that of surgical lithotomy, that it has in most instances a lower morbidity rate, and that it is much more acceptable for the patient. Patients undergoing endoscopic removal of calculi, regardless of the modality, have been shown to have much shorter hospitalizations and leave without the accompanying scar.

The first transurethral ureteroscopy was reported in 1929 by a Dr Hugh Young. At that time, an adult cystoscope was passed into the renal pelvis in a child with megaureters. However, the ability to reach the upper ureter and pelvis from below has only been realized with the development of extended length endoscopes of fine caliber. Visual endoscopy for stone removal has been quite successful at Massachusetts General Hospital, since its introduction there in 1983. Twelve of 23 (52%) among an initial 40 patients and 26 of 32 (81%) among the subsequent 41 patients were rendered stone free. As with any new instrument, a learning curve was seen and results improved with experience. The success of ESWL with stones above the pelvic brim has caused us to use the rigid ureteroscope for lower ureteral stones in most instances. Passage of the scope is preceded by dilation of the intramural tunnel and requires some finesse, but little morbidity ensues when the procedure is performed by an experienced surgeon.[5]

In February 1980, Dr Christian Chaussy[6] first used electrically generated focused shock waves to fragment stones within a human kidney without incision or puncture of the body. Since then, extracorporeal shock wave lithotripsy has rapidly become more widely available across the United States. At Massachusetts General Hospital, we have treated over 2,000 cases with exceptionally good results. The incidence of complications has been low.

Sepsis has occurred in 1-2% of patients and perinephric hematoma has occurred in fewer than 0.5%. The most common complication has been obstruction of the ureter with fragments from exceptionally hard stones or exceptionally large stone burdens. At present, the question remains as to which stones are better treated with ESWL alone and which should be debulked using percutaneous methods or dissolution therapy before shock waves are applied. There is a much higher incidence of obstruction when the stones are greater than 2 cm in size, and at present a rule of thumb holds that stones larger than that should be debulked using the percutaneous method. Residual fragments can then be "cleaned up" with ESWL.[7,8] Shock wave lithotripsy can also be used with ureteral calculi located above the pelvic brim. Venting with a ureteral stent is necessary in most instances in order to disimpact the calculus and allow optimum shock action. When a stent can bypass the stone or push it back into the renal collecting system, the success rate has been quite high, ranging from 74% to 100%.[1,9]

Endourology is a new specialty. Through the use of percutaneous methods, fiberoptic ureteroscopes, and ESWL, surgical lithotomy has become a rare operation in most hospitals. Many questions remain regarding these new modalities. Despite their attractiveness to patients, do these new surgical treatments result in a higher recurrence rate of urinary stones? Will percutaneous shock wave lithotripsy result in a significant loss of renal function? Does dilation of the ureterovesical junction prior to ureteroscopy result in reflux and stenosis of the ureter? Careful long term follow-up of these patients hopefully will provide an answer to these questions. In addition, we must continue in our efforts to treat not only the effects of disease, but also the causes. Only then will both open and closed surgical intervention become of historical interest for one of the oldest and most common diseases known to man.

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Hemophilus influenzae endocarditis: Managing the virtually unheard of

Bacterial endocarditis is a particularly serious infection which carries a substantial mortality and morbidity.[1] Clinicians who see patients with bacterial endocarditis understand that their management decisions (choice of antibiotics, duration of treatment, methods of monitoring therapy, etc) are of critical importance and that there is little room for error. As critical as these management decisions may be, the clinician can usually draw on personal experience and a vast accumulated literature of experience in the treatment of most cases of endocarditis. This is not true, however, when the organism proves to be a highly unusual one such as *Hemophilus influenzae*.

Personal experience with *H influenzae* endocarditis cannot form the basis for management; clearly it is a highly unusual medical career which includes caring for a second case of *H influenzae* endocarditis. Published reports of cases managed successfully are very rare and often have little in common with one another. It is not really what we know about *H influenzae* endocarditis that allows us to manage it intelligently. Rather it is what we know about *H influenzae* generally, and endocarditis generally, that allows us to recognize and manage *H influenzae* endocarditis by inference. There is vast potential for error in diagnosis and management by inference. Therefore, when the opportunity arises, it is crucial to establish that inferred recognition and management actually works. Herein lies the importance of the case report by Zwickler et al[2] in this issue of the *Journal*.

The next clinician who must diagnose and treat a patient with *H influenzae* endocarditis might learn several things from this case report. First, there is no diagnostic justice in this world, so the clinician must remain alert for the exceedingly improbable. In this case, for example, an adult (adults do not often get *H influenzae* disease of any kind) drug abuser (drug abusers generally inject skin or needle contaminant organisms, again, not *H influenzae*) gets endocarditis (while *H influenzae* comes to mind for infections like epiglotitis or pneumonia, whoever heard of

H influenzae endocarditis?[3]). This case illustrates that although *H influenzae* endocarditis is extremely rare, it is a recognized clinical entity which can occur even when the odds are overwhelming that it should not be the diagnosis.

Second, while we know that ampicillin is an effective drug for susceptible *H influenzae* infections of other organ systems generally, it is reassuring to note its success in the treatment of endocarditis in this case. With an organism sensitive to ampicillin, it was not necessary to resort to more innovative antibiotic regimens for successful treatment. The clinician treating a similar case would be well advised to follow the example here and administer large doses of intravenous ampicillin every four hours. No report of experience for the treatment of ampicillin resistant *H influenzae* endocarditis is published. In that circumstance, the clinician would be forced to manage by inference, and select antibiotics based on experience with ampicillin resistant *H influenzae* infections of other organ systems.

Third, endocarditis generally responds to a regimen of six weeks of intravenous antibiotics. There is no *a priori* reason to expect that *H influenzae* endocarditis should be different, yet it is reassuring to read a report of success with this standard duration of therapy. This suggests that *H influenzae* is not unusually difficult (in terms of the length of treatment required) to eradicate from the endocardium. Whether or not it is any easier to eradicate will likely remain an unanswered question. *H influenzae* endocarditis occurs so rarely that it is unlikely that other routes of antibiotic administration or short duration of therapy could ever be studied in any meaningful way. Therefore, it seems prudent to follow the example of this case report and administer intravenous antibiotics for six weeks in cases of *H influenzae* endocarditis.

H influenzae endocarditis is something of a medical curiosity, and perhaps the general interest in the occurrence of such an unusual disease justifies reporting it. However, this case report also serves a more pragmatic purpose. It provides confirmation that what we think should succeed in the management of *H influenzae* endocarditis actually has succeeded for a specific patient. Physicians who otherwise must feel their way along in this diagnostic and therapeutic no-man's land perhaps can find some guidance in this report, in that others have successfully passed this way before.

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Adult respiratory distress syndrome in adolescents due to aspiration of gastric contents

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ABSTRACT. Adult respiratory distress syndrome (ARDS) has recently been described in children; it has a high mortality, as in adults. Aspiration of stomach contents is a common cause of ARDS and is associated with increased morbidity and mortality in adults. We describe five adolescents who survived ARDS following gastric aspiration. Eighteen months after ARDS they have continued to show improvement in pulmonary function and gas transfer. ARDS following aspiration of stomach contents has an excellent prognosis among young people who experience single organ failure and receive aggressive ventilatory support.

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Adult respiratory distress syndrome (ARDS) is characterized by pulmonary edema that is not associated with cardiac function. It is associated with a mortality rate of greater than 50%.[1] Descriptions of ARDS in adolescent patients have been limited to individual case reports and descriptions of adolescents in series on adults. There have only been a few papers describing ARDS in children (several weeks old to 17 years of age); the mortality rate has been reported to be as high as in adults: 40–60%.[2–4]

Aspiration of stomach contents is a major cause of ARDS in both adults[3–5] and children.[2–4] In adults, ARDS following gastric aspiration has a high mortality rate.[6–9] The morbidity and mortality of this disorder in adolescents is thought to be low. We describe the immediate outcome and 18-month follow-up of five consecutive adolescent patients who survived ARDS caused by gastric aspiration.

PATIENTS AND METHODS

The diagnosis of ARDS in all patients was based on clinical, roentgenographic, and physiologic criteria, which included hypoxemia ($Pa_{O_2} < 50$ mm Hg with $F_{I_{O_2}} \geq 0.50$), diffuse alveolar infiltrates on chest film, pulmonary capillary wedge pressure (PCWP) ≤15 mm Hg, and static lung compliance <50 mL/cm water.

Arterial and Swan-Ganz catheters were inserted in all patients, and serial measurements were taken of the arterial oxygen tension (Pa_{O_2}), pulmonary arterial pressure (PA), mean pulmonary arterial pressure ($\overline{PA}$), PCWP, mixed venous oxygen tension ($P\bar{v}_{O_2}$), cardiac output, and static lung compliance. All patients received ventilatory support with the use of positive end-expiratory pressure (PEEP). Levels of PEEP were adjusted to safely reduce the $F_{I_{O_2}}$. The PCWP was read at end expiration and was maintained between 8 mm Hg and 14 mm Hg in all patients.

Nutritional support was instituted in all patients within 24 hours of admission. The patients received 1,200–2,000 calories/day via Keo nasogastric feeding tubes.

Case 1. A 14-year-old boy was admitted to the emergency room for an episode of generalized seizure. His medical history was unremarkable, and he was not taking any medications. In the emergency room, he had another generalized seizure, and he vomited during the administration of intravenous phenytoin. Respiratory distress and cyanosis followed immediately. The cyanosis disappeared following intubation and suctioning; however, his respiratory rate remained at 35/min. There was no further evidence of seizures, and the chest roentgenogram was not abnormal. An arterial blood gas study obtained while the patient was receiving 40% oxygen by T-piece revealed a Pa_{O_2} of 82 mm Hg. Because of wheezing in the upper lobe of the right lung one hour after aspiration, flexible fiberoptic bronchoscopy was performed to rule out aspiration of food material. The posterior tracheobronchial walls were markedly erythematous and friable, as were the orifices to the lower lobe of the right lung. No foreign material was noted.

The patient was transferred to the intensive care unit. Repeat arterial blood gas studies demonstrated a Pa_{O_2} of 55 mm Hg. Mechanical ventilatory support was instituted. A repeat chest roentgenogram taken five hours after aspiration revealed diffuse bilateral infiltrates.

The result of an arterial blood gas test on 100% oxygen via assist-control ventilation was 85 mm Hg. The PA was 22/12 mm Hg; $\overline{PA}$, 15 mm Hg; and PCWP, 12 mm Hg. Static lung compliance obtained while the patient was on the ventilator was 32 mL/cm water. Ventilatory support with PEEP for ARDS was instituted. Pharmacologic therapy included maintenance doses of phenytoin to prevent further seizures.

During a seven-day period, the patient's pulmonary status improved, as manifested by a progressive rise in Pa_{O_2}, reduction of PEEP (maximum of 12 cm water), clearing of infiltrates, and no further need for ventilatory support. He was discharged from the hospital 16 days after admission, while still receiving phenytoin for an idiopathic seizure disorder. Pulmonary function tests one month following ARDS demonstrated a mild restrictive pattern, with a mild reduction in gas transfer as noted in the single breath carbon monoxide diffusing capacity and Pa_{O_2} while exercising. These values and follow-up studies are shown in Table I.

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Case 2. A 14-year-old girl was admitted to the emergency room following a suicide attempt by hanging. On physical examination she was cyanotic with a rope burn around her neck, and chest wall motion was barely visible. Her blood pressure was 110/80 mm Hg; heart rate, 110/min. A nasotracheal tube was inserted, and she was placed on 100% oxygen.

Suctioning through the tube disclosed food particles that had been aspirated. Flexible fiberoptic bronchoscopy revealed friable mucosa along the posterior tracheobronchial walls. In addition, small peanut fragments were removed from an orifice of the lower lobe of the right lung. A chest roentgenogram taken shortly after intubation and prior to bronchoscopy revealed bilateral infiltrates. The PaO_2 on 100% oxygen was 98 mm Hg. The PA was 38/10 mm Hg; $\overline{PA}$, 14 mm Hg; and PCWP, 7 mm Hg. Static lung compliance was 37 mL/cm water. Ventilatory support with PEEP (maximum of 15 cm water) for ARDS was instituted. Pancuronium bromide and diazepam were also employed to control marked agitation and to assure patient/ventilator synchrony.

The patient's condition was complicated by a pneumomediastinum, which did not progress to pneumothorax or subcutaneous emphysema. Her hospital stay was otherwise uneventful for the nine days of ventilatory support. She had complete neurologic recovery and was discharged to a psychiatric institute. A month after admission, her pulmonary function tests, single breath carbon monoxide diffusing capacity, and PaO_2 on exercise demonstrated mild restriction and gas transfer abnormalities (Table I).

Case 3. A 17-year-old girl with a known history of bulemia was admitted to the hospital for acute respiratory distress following an episode of self-induced vomiting. On physical examination she was cyanotic, with cool extremities. Her blood pressure was 100/60 mm Hg; heart rate, 130/min; and respiratory rate, 40/min and shallow. A nasotracheal tube was inserted, with improvement in the patient's color. However, suctioning demonstrated blood streaked secretions. Flexible fiberoptic bronchoscopy disclosed marked tracheobronchial erythema and friability, as well as petechial hemorrhage in the orifices to the upper lobe of the right lung. No foreign material was noted in any of the orifices to the major lobes. The PaO_2 taken after intubation and mechanical ventilation on 100% oxygen was 55 mm Hg. A chest roentgenogram revealed diffuse infiltrates in both lungs—greater in the right lung. The PA was 30/8 mm Hg; $\overline{PA}$, 17 mm Hg; and PCWP, 11 mm Hg. Static lung compliance was 29 mL/cm water. Ventilatory support with PEEP for ARDS was instituted, including the use of dobutamine to augment cardiac output during successive increases in PEEP (maximum of 18 cm water), while maintaining the PCWP between 11 mm Hg and 16 mm Hg.

Steady improvement occurred, with discontinuation of ventilator therapy after nine days. One month following aspiration, the patient's pulmonary function tests, single breath carbon monoxide diffusing capacity, and PaO_2 on exercise were consistent with moderate restrictive disease and mild impairment of gas transfer (Table I). She received treatment at a private psychiatric institute for four months and was then discharged to her home.

Case 4. A 17-year-old girl was admitted to the emergency room in acute respiratory distress following an episode of self-induced vomiting achieved by inserting a bent clothes hanger down her throat and into the stomach in order to "churn" the stomach contents. In the emergency room, she was cyanotic, with a blood pressure of 120/80 mm Hg; heart rate, 122/min; and respiratory rate, 38/min. Examination of the lungs revealed diffuse rhonchi. An endotracheal tube was inserted together with a T-piece delivering 100% oxygen. Arterial blood gas studies revealed a PaO_2 of 112 mm Hg, and a chest roentgenogram demonstrated diffuse infiltrates. Suctioning from the endotracheal tube disclosed food debris. Flexible fiberoptic bronchoscopy demonstrated friability and erythema of the posterior tracheobronchial tree, with small food particles in the orifices to the upper lobe of the right lung and lower lobe of the left lung. Suctioning of these particles was carried out without prior lavage.

During the following two hours, while receiving 100% oxygen via a T-piece, the patient's respiratory rate increased to 50/min, with deterioration in the PaO_2 to 59 mm Hg. She was placed on a ventilator of which the static lung compliance was 22 mL/cm water. Ventilatory support for ARDS was delivered over an eight-day period, with levels of PEEP ranging to 14 cm water. A follow-up chest roentgenogram showed minimal infiltrative markings in the lower lobe of the right lung at the time of discharge to a psychiatric facility. One month after admission for acute respiratory distress, pulmonary function tests showed moderate restrictive disease with mild impairment of gas transfer, as noted on the single breath carbon monoxide diffusing capacity and PaO_2 on exercise (Table I).

Case 5. A 17-year-old boy was admitted to the emergency room with a traumatic closed fracture of the left radius. To reduce the fracture, general anesthesia was administered, with moderate inspiratory stridor noted shortly therafter. In the process of having an endotracheal tube inserted, the patient vomited stomach contents, with some being aspirated as noted on suctioning of the endotracheal tube. The patient's respiratory rate increased to 60/min. Arterial blood gas studies during delivery of 60% oxygen via a T-piece revealed a PaO_2 of 57 mm Hg. A chest roentgenogram demonstrated minimal, bilateral diffuse infiltrates. Flexible fiberoptic bronchoscopy disclosed extensive tracheobronchial erythema and friability, with no food particles suctioned.

The patient was transferred to the intensive care unit. While receiving mechanical ventilation with 80% oxygen, the PaO_2 was 54 mm Hg, with a static lung compliance on the ventilator of 30 mL/cm water. The PA was 35/11 mm Hg; $\overline{PA}$, 18 mm Hg; and PCWP, 10 mm Hg. Ventilatory support for ARDS was instituted, with the patient requiring as much as 22 cm water of PEEP to reduce the FI_{O_2} to 0.55. Continued respiratory support was maintained throughout a ten-day period, with no complications. The left radius was reduced and placed in a cast while the patient was on the ventilator. On discharge from the hospital, his chest roentgenogram was clear. Pulmonary function tests one month after admission revealed moderate restriction and mild impairment to gas transfer, as manifested in the single breath carbon monoxide diffusing capacity and PaO_2 on exercise (Table I).

TABLE I. Pulmonary Function and Gas Transfer at One-, Six-, 12- and 18-Month Intervals Following ARDS

Patient	Forced Vital Capacity (% Predicted)	Forced Expiratory Volume in 1 sec (% Predicted)	Total Lung Capacity (% Predicted)	Functional Residual Capacity (% Predicted)	Single Breath Carbon Monoxide Diffusing Capacity (% Predicted)	Rest PaO_2 (mm Hg)	Exercise PaO_2 (mm Hg)
1	68,77,86,85*	70,72,81,85	71,78,80,86	61,73,82,84	67,80,83,80	81,89,86,91	70,80,93,92
2	70,83,89,88	79,80,86,82	73,82,93,91	69,77,84,89	68,69,69,72	76,84,87,80	69,80,79,75
3	64,82,88,—	73,74,79,—	61,79,89,—	63,75,85,—	66,71,75,—	79,87,96,—	72,82,90,—
4	73,85,92,90	80,82,88,92	72,86,89,91	75,83,90,93	61,74,86,83	72,79,83,88	64,70,80,86
5	60,—,82,89	67,—,74,79	57,—,80,83	59,—,81,80	69,—,78,75	72,—,89,93	70,—,84,86

* Values are given for one, six, 12, and 18 months, respectively.

Discussion

ARDS is now recognized as a serious pulmonary disorder in adolescents.[2-4] Only a few published papers have reported this entity. The predisposing conditions in young people appear to be similar to those in adults.[2-5] These risk factors include sepsis, aspiration, hypotension, and near drowning. Aspiration of gastric contents is a major cause of ARDS in adults,[5] and has recently been recognized in the literature as a cause of ARDS in adolescents.[2-4]

This report demonstrates that following aspiration of stomach contents and the development of ARDS, adolescents have an excellent short term and 12-month recovery. Determination of the cause of ARDS in all five patients was based on the following: their predisposing conditions were likely to be associated with gastric aspiration,[7] and bronchoscopic examinations established a definitive diagnosis.[9] There are several probable reasons for these patients' favorable recoveries: the nature of the material aspirated; the age of the patients; the occurrence of only single organ failure; and the aggressiveness of accepted supportive therapy.

Although these patients all had ARDS secondary to gastric aspiration—which included food particles in two patients—the pH and volume of the stomach contents were not known. A critical pH below 2.5 is believed to be associated with severe lung damage in humans.[10,11] Recently, however, in dogs, aspiration of stomach contents with a pH greater than 2.5 was associated with harmful effects,[12] contradicting the common belief that aspiration of such material is benign.[13] In addition, experimental studies have shown an increased mortality with larger aspirated volumes.[14] In 1976, Bynum and Pierce[7] attempted to correlate human survival with experimental evidence of the effects of gastric content pH and volume, as well as the presence of complicating bacterial infection.[7] The authors categorized patients into one of three aspiration patterns related to outcome. In their study, 62% of patients had rapid clinical and radiologic improvement in an average of 4.5 days (range, 2–16 days). The five patients described in this report seem to fit into this category; they were off of ventilatory support and had roentgenographic improvement in an average of 8.6 days (range, 7–10 days). The two other patterns described by Bynum and Pierce were associated with a high mortality rate. One group of patients (12%) had hypotension and apnea, and all died immediately. The other patients (26%) initially did well, but then had complicating bacterial infection, with 60% of this group having a fatal outcome. Accordingly, when shock, apnea, severe hypoxemia, and complicating infection are absent, it appears that a more favorable prognosis may be anticipated.

A second reason for survival of all five patients reported here may be related to their young age, as suggested in two reports on aspiration. In Bynum and Pierce's[7] paper, patients who died had a mean age of 47.5 years, versus the survivors with a mean age of 26.5 years. In the study by Lewis et al,[8] the mean age of patients who died was twice that of survivors, 70.6 years versus 34.6 years. In reviewing the three manuscripts that describe the 53 children with known causes of ARDS, it appears that two children definitely aspirated stomach contents, and three possibly aspirated stomach contents.[2-4] The two who were known to have aspirated survived, whereas the three with possible aspiration had another acute condition,[4] and it is not clear from the paper whether any of them survived (17 out of 18 patients died in this series). The survival of the five patients reported here, as well as the supporting findings in the literature, suggest that younger patients have a better survival rate when gastric aspiration causes ARDS.

A recent finding describes the influence of multiple organ system failure on survival among patients with ARDS. Bell et al[15] found that patients with ARDS and multiple organ system failure had a high mortality rate despite extensive supportive therapy. Failure of the central nervous, coagulation, endocrine, gastrointestinal, and renal systems was more frequent in those patients who died. In the paper by Pfenninger et al,[3] on 20 children with ARDS, additional organ system failure was common, and children who subsequently died had more multiple organ system failure or dysfunction. In the report by Holbrook et al[4] on 18 children with ARDS, 17 died, and the authors concluded that improvement in overall mortality awaits developments in the treatment of organ system failure. None of the five adolescents described in this report had additional organ failure beyond the respiratory system, indicating that an excellent prognosis may be expected if other organ systems do not become compromised during the course of ARDS.

Another reason why these five patients had a favorable outcome is that prompt, aggressive, accepted methods of ventilatory supportive care were instituted. Respiratory and hemodynamic measures were taken on a serial basis, and the data were interpreted by an intensive care specialist. Swan-Ganz and arterial catheters were removed as soon as the patient's condition was thought to be stable and progressing in a favorable direction, so that complications and infections could be minimized. No patient received prophylactic, steroid, or antibiotic therapy,[13] and all patients received nutrition early in the course of their illness. Although adolescents may be expected to do well, it is possible that this total supportive approach may further minimize the development of additional organ dysfunction.

In addition to the excellent short term prognosis for these five patients, further findings indicate that following ARDS, serial pulmonary function improved over the course of 18 months (Table I). However, hope for complete return of normal pulmonary function and gas transfer must be circumspect. There have been a number of papers describing pulmonary function in adults following ARDS, with preliminary reports having been favorable.[16,17] However, following the analysis of more sensitive parameters of pulmonary function over a longer period of time, it appears that reports of the encouraging clinical and functional outcome of ARDS survivors may have been premature.[18] Abnormalities in gas transfer may persist,[19] and the diffusing capacity may take four years to return to normal.[20] In addition, ARDS is characterized by partial or complete disruption and even disappearance of much of the pulmonary vascular bed.[21] Gas transfer abnormalities have persisted in several patients for up to 18 months after ARDS, as reflected in the lower than predicted diffusing capacity and fall in oxygen tension on exercising. Only long term follow-up of these patients will

answer the question as to ultimate outcome, but the prognosis appears favorable.

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See also pp 508–510.

FROM THE LIBRARY

THE NEW MARINE HOSPITAL

SICK SEAMEN TO BE QUARTERED ON BEDLOE'S ISLAND

For more than two years past the authorities of the United States Medical Marine Service have been making strenuous efforts to get possession of Bedloe's Island, in New York Harbor, for the purpose of establishing thereon a hospital for the treatment of those coming under their care in this locality. The Surgeon-General of the Marine Hospital Service, in his report for the year 1876–7, urged the selection of the island as a site for a hospital, and application was immediately made for the transfer of the island to the Marine Services for that purpose. The island, however, having been designated, by resolution of Congress passed March 3, 1877, as the site for the colossal statue of "Liberty Enlightening the World," the War Department refused to relinquish any portion of it until the site of the statue had been selected. The highest portion of the westerly side of the island is occupied by old Fort Wood, and this is generally conceded to be the proper site for the statue. Finally, the War Department gave orders for the transfer of the island to the Treasury Department, and on the 1st of the present month it was turned over to the Marine Service, and the work of transformation for the accommodation of its new occupants was at once begun.

This will be the first institution of the kind ever established in this City, and will supply a want long felt here. The Government has built marine hospitals in several places, but New York, Philadelphia and Baltimore, three very important points in a hospital point of view, have thus far been left unprovided for. For that reason, all the patients coming under the care of the Marine Medical Department in this City have been sent to the various hospitals of New York and Brooklyn, and to the Seamen's Retreat Hospital on Staten Island. The average number of patients thus provided for has been from 200 to 250 per month. The selection of Bedloe's Island is considered one of the very best that could have been made, on account of its healthy location and nearness to the City. The island covers an area of 12 acres, is 2,950 yards from the Battery, is surrounded by water, and, being well elevated, the patients will always have the benefit of pure sea air, which will render its location as healthy and salubrious as can be desired. The records of the Army, covering a period of many years, show it to have been the healthiest military post in the harbor.

Besides being occupied as a United States military post, Bedloe's Island was also used as a place of execution of all offenders against the United States Government. It was there that Hicks, the pirate, was hanged a number of years ago. During the late war it was used for Army hospital purposes, and frequently was occupied by as many as 1,000 patients at a time. It was evacuated by the United States troops in April last, and since that time the garrison has consisted of one old Orderly-Sergeant in charge of the fort and Gen. Hancock's mule. Yesterday the mule was taken away, leaving only the Sergeant, who will, for the present at least, remain at his post.

(*New York Times*, August 12, 1879, p8, col 1,
courtesy of Florence Kavaler, MD)

Health care patterns of non-urgent patients in an inner city emergency room

BARBARA HABENSTREIT, MA

ABSTRACT. Interviews were conducted with 56 non-urgent emergency room (ER) patients in a large, inner city public hospital in order to develop an understanding of how non-urgent patients used emergency rooms in relation to other sources of health care available in the community. Thirteen patients (23%) reported that hospital emergency rooms were their sole source of health care, whereas 43 patients (77%) were multiple-source users who relied on clinics and private physicians (defined as such by the respondents) as well as emergency rooms. However, more than half of the latter group "usually" went to emergency rooms for routine problems. Thus, the ER was the *main* source of primary care for 63% of the respondents. All appeared to regard it as an appropriate source.

In deciding which type of provider to use in noncrisis situations, multiple-source users balanced such factors as cost, quality of medical care, accessibility, prior experience, convenience of location, and availability of a pharmacy.

When a private physician was used, often it was because the medical problem was perceived as potentially serious or frightening, or because pain was present and the patient wanted to avoid the long wait that could be expected in an emergency room. Clinics were used mainly for monitoring chronic problems or special conditions such as pregnancy.

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Use of hospital emergency rooms by patients with non-urgent health problems has escalated sharply during the past 25 years. While the trend has occurred nationwide, it has been most pronounced in inner city neighborhoods with large indigent and minority populations who rely on emergency rooms as their "family physician." [1,2]

On a nationwide basis, it is estimated that non-urgent patients account for over 50% of all emergency room visits.[3] Only about 12% of visits are considered true emergencies that necessitate immediate attention.[4] The rest fall into various intermediate categories.

In low income, inner city areas, individual hospitals report higher frequency of use of emergency rooms for routine care. At Kings County Hospital, a public facility located in a low income, predominantly black and Hispanic section of Brooklyn, New York, clinically non-urgent cases comprise more than 60% of emergency room visits, with true emergencies accounting for 10% (unpublished reports by second year medical students, submitted to the Department of Preventive Medicine and Community Health, SUNY Health Science Center at Brooklyn, 1982). According to the director of Community Health Services and Ambulatory Care of Brookdale Hospital Medical Center (personal communication, April 1982), the figures are similar in the emergency room at that facility, a voluntary institution located a short distance from Kings County Hospital and also serving predominantly low income and minority communities.

The Kings County Hospital emergency room is mandated to provide treatment to all who request it, regardless of ability to pay. Patients who have no money at the time of a visit will be billed afterwards, but the hospital collects just a small fraction of costs that emergency room patients are supposed to pay themselves. The standard fee for a visit at the time of the survey was $82, but few patients actually paid that amount. For those without Medicaid, Medicare, or other insurance to cover the cost, a sliding scale fee based on income can be negotiated.

The Kings County Hospital emergency room is very heavily used, with a patient load of about 600 daily. Waiting time for non-urgent patients averages about three to four hours. As might be expected of such a large and overloaded facility, medical treatment is impersonal and patients remain relatively anonymous. Continuity of care is not possible, making it (or any ER) ill-suited for the role of primary care provider.

Much of the population relying on the Kings County Hospital ER for routine care is foreign-born, consisting of immigrants from the Caribbean, South America, and elsewhere. For New York City as a whole, 1980 census data lists about 300,000 non-Hispanic Caribbean immigrants, but estimates of the undocumented and uncounted raise the total to more than 600,000.[5] The majority of the Caribbean population lives in Brooklyn.

Many of the undocumented earn subsistence wages or are unemployed, yet are ineligible for Medicaid coverage because of their questionable immigration status. (A recent judicial decision declaring such persons Medicaid-eligible is being challenged.)

This study was conducted in partial fulfillment of the degree of Master of Arts in Medical Anthropology, under the auspices of the Graduate Faculty of The New School for Social Research, New York, NY.

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Even those who are documented often lack health insurance, as do many low income Americans who earn slightly too much to qualify for Medicaid, cannot afford to pay for private health insurance, and have jobs that do not provide it. These "working poor" comprise a substantial portion of the patient load in the Kings County Hospital emergency room. Reports indicate that about 40% of all outpatients (in the clinics and the emergency room) have no health coverage (unpublished reports by second year medical students, submitted to the Department of Preventive Medicine and Community Health, SUNY Health Science Center at Brooklyn, 1982).

It has been widely reported that low income people, many of whom live in medically underserved areas, use emergency rooms for routine care because they have no other place to go. But the area of Brooklyn surrounding Kings County Hospital is medically well-endowed, with five hospitals located within a relatively short distance from each other, and numerous clinics and Shared Health Facilities (SHFs) (sometimes labeled "Medicaid mills"). However, neighborhood pharmacies are rare, as are traditional, community based private physicians (although adequate numbers practice in middle class neighborhoods not far away).

Given a relative abundance of public and private medical facilities in the midst of a large, low income and/or medically indigent population, a survey was undertaken to explore the health care behavior of US-born and foreign-born patients who relied heavily on a public hospital emergency room for routine care. Their use of the emergency room was examined not in isolation but as part of their broader care-seeking patterns, in order to yield an understanding of how such patients used ERs in relation to other sources of health care available in the community.

Interviews were loosely structured and exploratory in nature, intended primarily to encourage patients to talk freely about how they utilized the health care system. Although the sample size was small, the responses provided useful insights into patients' behavior.

Methods

Personal interviews were conducted with 56 non-urgent patients who had been screened in triage and were waiting to see a doctor in the Kings County Hospital emergency room. The loosely structured interviews were conducted by one researcher over a period of two months in 1982, and varied in duration from 20 to 50 minutes, depending on the responsiveness of the patients.

All patients were asked why they had come to the emergency room; if they had ever been there before; if they had other places they could go when they were sick; and if so, how they made the choice about where to go during each illness episode. These questions and several others formed the core of the interviews; additional questions were asked spontaneously, in response to patients' remarks. (Eight additional interviews were not included in the survey because they were interrupted when the patients were called in for examination.)

Only one patient declined to be interviewed when approached, saying he felt too sick. Most of the others appeared eager for conversation, if only to alleviate boredom during the long wait to see a doctor.

All of the interviews were held on weekdays, between 9 AM and 5 PM, when other types of health care facilities were also open. This indicated that the respondents had exercised some degree of choice in coming to the Kings County Hospital emergency room, and were not there solely because all other places were closed. None of the respondents appeared to have critical health problems that necessitated immediate attention; nor did they themselves claim to be in the midst of a health emergency (although three of them did appear to be in some distress). This further supported the observation that the respondents had been able to exercise some choice about where to go for treatment.

On a nationwide basis, 60% of all patients who come to emergency rooms *believe* they have an emergency problem, although physicians may not evaluate it as such.[6] However, of the non-urgent patients interviewed at Kings County Hospital, not one described the current problem as an emergency. Some had used the ER during past crises, but they made a distinction between those urgent situations and their more usual, routine visits.

No systematic attempt was made to correlate routine use of the emergency room with income, employment status, health insurance coverage, or ability to pay. Direct questions about the respondents' ability to pay for health care tended to arouse suspicions about the purpose of the interviews, and to inhibit patients' willingness to talk freely about why they had chosen an emergency room for treatment. However, when not directly asked, many patients volunteered information about the financial factors that influenced their decision making processes during illness episodes. To preserve anonymity and further encourage open conversation, respondents were never asked their names. The researcher was identified as an employee of SUNY Health Science Center at Brooklyn (formerly Downstate Medical Center), who was not connected with Kings County Hospital.

The Respondents. Thirty-one of the 56 respondents were US-born, and all but one were black. The remaining 25 were immigrants: 9 were Haitians; 9 were Hispanics; and 7 were from the English-speaking Caribbean islands. There were 34 women and 22 men, which roughly corresponds to the female/male ratio commonly seen in urban emergency rooms. (The patient ratio in the Brookdale Hospital emergency room, for example, is 65% female/35% male.) The average age of the respondents was 30–35. In all cases, respondents who could not speak English were accompanied by a friend or family member who served as a translator.

Results

A large majority of those interviewed were relatively frequent emergency room users. Only three of the 56 patients (5%) reported that this was their first visit to the Kings County Hospital emergency room, whereas 39 patients (70%) had been there three or more times (usually more) during the previous two years (Table I).

Almost half of those who frequented the Kings County Hospital emergency room reported having utilized other hospital emergency rooms as well. Only one patient reported no prior use of any emergency room.

Thirteen respondents (23%) said that hospital emergency rooms were their sole source of health care (Table II). Forty-three respondents (77%) were multiple-source users who went to clinics and private physicians as well as to emergency rooms. However, 22 of the patients in this latter group said they "usually" relied on emergency rooms for routine problems (Table III). This meant that for 35 of the respondents (63%), emergency rooms were the sole or main source of health care.

TABLE I. Prior Use of the Kings County Hospital (KCH) Emergency Room by Non-Urgent Patients

Use of KCH ER	No. of Patients	No. Who Also Used Other Hospital ERs
First-time use	3 (5%)	2
One prior visit	7 (12.5%)	4
Two prior visits	7 (12.5%)	3
Three or more prior visits	39 (70%)	18
Total:	56 (100%)	27 (48%)

TABLE II. Use of Ambulatory Care Providers by Non-Urgent Patients Seen at the Kings County Hospital Emergency Room

	Providers	No. of Patients
Single-source users	Emergency rooms only	13 (23%)
Multiple-source users	Emergency rooms and clinics	21 (38%)
	Emergency rooms and private MDs	12 (21%)
	Emergency rooms, clinics and private MDs	10 (18%)
Total:		56 (100%)

The interviews revealed similar patterns of emergency room use by the US-born and the foreign-born as a whole. When specific ethnic groups were looked at, however, Haitians appeared to have less access to health care outside an emergency room than the other ER users (Table IV).

This supported findings of a recent study of Caribbean immigrant women who attended health fairs in Brooklyn.[7] It suggests certain possibilities: that Haitian immigrants may be poorer than the other low income groups; that they are less likely to have any form of health coverage; and that a greater number of them may be undocumented and afraid to use facilities where they would not be as anonymous as in an emergency room.

In general, however, all the respondents could be classified into two main groups: those who relied exclusively on hospital emergency rooms for all their ambulatory health care needs, and those who frequented clinics and/or private physicians in addition to ERs (multiple-source users).

Patients Using Emergency Rooms Exclusively. Thirteen respondents had never gone anyplace other than to a hospital emergency room for ambulatory care, and seven of the 13 had used only the Kings County Hospital emergency room.

Of the latter group, all lived near Kings County Hospital, and four mentioned that their mothers had regularly taken them to the ER while they were growing up. As adults they continued to rely solely on the Kings County Hospital emergency room, and two now took their own children there, to the pediatric ER. All seven said they felt comfortable at Kings County Hospital, they were familiar with the system, and their perception of the medical care was that it was generally good. Their main complaint was the long waiting time at each visit.

These patients relied exclusively on the Kings County Hospital emergency room primarily because of early socialization, habit, and convenience, rather than through the exercise of selective judgment. (Other research also suggests the importance of early socialization among regular ER users.[8]) They had no basis on which to compare medical treatment in the Kings County Hospital ER with treatment in other facilities because they had never been anyplace else, as far as they could recall. Their experience with the health care system was extremely limited.

The six other patients who used emergency rooms for all their outpatient care did not confine themselves to Kings County Hospital. Some regularly used and/or preferred at least one other emergency room; others had sampled up to three different emergency rooms and sometimes utilized them for "second opinions." Most of these patients preferred Kings County Hospital because they felt it offered the best medical care (ie, the best doctors and most advanced technology). They usually went there even though the hospital's location was not necessarily convenient for them and they experienced longer waits there than in other emergency rooms.

TABLE III. "Usual" Source of Health Care Among 56 Patients Interviewed at Kings County Hospital Emergency Room

Place of Birth	Use Only ERs	Usually Use ERs	Usually Use Clinics	Usually Use Private MDs	Total
US-born	7	13	6	5	31
Foreign-born	6	9	7	3	25
Total	13 (23%)	22 (39%)	13 (23%)	8 (14%)	56

Multiple-Source Users. Among the 43 multiple-source users, the most common reasons for selecting an emergency room during their current illness episode were: cost; quality of care; accessibility (no need to wait for an appointment or office hours); had received bad/ineffective treatment elsewhere; convenience of location; hospital pharmacy available (Table V).

Whereas the 13 patients who utilized only emergency rooms would go there for all health problems, whether minor or severe, the multiple-source users tended to visit ERs mainly for routine illnesses or for initial diagnosis and treatment. The health problems that had prompted their current visit included sore throats, fevers, respiratory infections, vaginal infections, postmiscarriage checkup, backaches, hypertension checkup, and possible ulcer flare-up. Those with colds or flu-like symptoms had come mainly to get medication.

Twenty-two of the multiple-source users said their "usual" provider of health care for such problems was an emergency room (Table III). All seemed to regard it as an appropriate source, rather than one they had turned to as a last resort.

The 21 patients who mainly used other sources said they had come to the ER because their own physician did not have office hours or because they could not get a clinic appointment quickly enough.

Twenty-two of the multiple-source users reported having gone to private doctors on some occasions (Table II). Eight said that their usual source of health care was a private physician (Table III), and they relied on emergency rooms only as a backup when their own doctor did not have office hours. The other 14 used emergency rooms as their regular source of care, but turned to private doctors for more serious or special problems, usually weighing the nature of the illness episode against the availability of their resources. The more serious they considered the problem to be, the more likely they were to spend the money for private care, if they were able to afford it. For chronic conditions, they relied mainly on clinics.

Respondents' reasons for deciding whether to go to an emergency room or to a private doctor are illustrated by the following cases:

A woman who regularly used the emergency room for mild, temporary illnesses, and who was currently there for knee pain, said she had used a private specialist when she had had a serious eye injury and was very concerned about it. Another woman who was in the ER for "the flu" said that when she had "trouble with my tubes" and needed tests, she went to a private physician who could "follow my case." A man with a "very bad throat" had come to the ER for treatment, but he used a private doctor for his sinus and hypertension problems. Respondents such as these said they could not afford to go to a private doctor for all their health needs, so they used an emergency room for conditions they felt were temporary and/or relatively minor.

Many appeared to regard the emergency room as "free." At least ten of the respondents had Blue Cross, union, or other health insurance plans that paid for emergency room treatment but did not cover other types of ambulatory care. These patients indicated that they used an emergency room most of the time, and only occasionally went to private physicians.

Several other patients, who apparently had no health coverage, also referred to the ER as "free." When the interviewer mentioned the $82 fee, they explained that they did not have to pay right away in the Kings County Hospital emergency room; they could be billed later if they had no money. Private physicians, by contrast, had to be paid "up front" and were "expensive."

Two patients said they had received better health care in the past, when they were unemployed and on Medicaid, than now when they were working. Both had been using private doctors who accepted Medicaid reimbursement. After the patients found jobs, however, they lost their Medicaid coverage and could not afford private physicians.

One of these patients was in the emergency room with a severe backache and hoped to get medication to ease the pain. His back had been hurting for a few days, but he had delayed going for treatment

TABLE IV. Emergency Room Use by Ethnicity Among 56 Patients Interviewed at the Kings County Hospital Emergency Room

Ethnicity	Use Emergency Rooms Exclusively	Usually	Usually Use Clinics and/ or Private MDs	Total
Haitian	4 (44%)	3 (33%)	2 (22%)	9
Hispanic	1 (11%)	4 (44%)	4 (44%)	9
English-speaking Caribbean	1 (14%)	2 (29%)	4 (57%)	7
Total foreign-born	6 (24%)	9 (36%)	10 (40%)	25
Total US-born	7 (23%)	13 (42%)	11 (35%)	31
Total:	13 (23%)	22 (39%)	21 (38%)	56 (100%)

because it meant he would lose a day's pay. Now the pain was too severe to ignore. If he could not get relief in the ER, he would "wait until payday" (three days later), when he would have money to visit the private doctor he had used when he had Medicaid coverage.

This patient had already been waiting in the emergency room about two hours at the time the interview began, and when it ended 40 minutes later he still had not been called. Because of the long waiting time that can be expected in an emergency room, several patients said they tried to avoid using an ER when they were in severe pain or felt very sick. If at all possible, they would go to a private doctor during such episodes.

One woman reported that several months earlier she had come to the Kings County Hospital emergency room with an "urgent problem." After waiting four hours, she left and went to a private physician. She said she always takes her children to a private physician, but "I can't afford it for myself very often." She had come to the ER that day to get treatment for a vaginal infection. (Another woman also reported having left the ER to go to her private doctor on a previous occasion, when she had been kept waiting too long.)

Many patients expressed the view that the Kings County Hospital emergency room had "good doctors" and "good equipment." Fourteen respondents specifically stated that the quality of medical care was one of the main reasons why they came to Kings County Hospital. Nevertheless, private physicians were generally preferred because of the shorter waiting time and more personalized attention. Such factors became more significant when illnesses were perceived as serious or frightening.

Patients also complained of rude or nasty treatment by clerical intake personnel in the Kings County Hospital emergency room. Several said that nurses had also been rude; two complained of rude physicians. The likelihood of being treated badly, particularly by emergency room clerks, was an important reason why patients preferred going to private physicians. Nevertheless, their resources were too limited to permit them to do so unless they thought their illness was serious enough to justify the expenditure.

Thirty-one respondents in the emergency room reported that they also utilized clinics; for 13 of these patients, clinics were the usual source of care (Tables II, III). Many of their routine visits to the Kings County Hospital ER would not have occurred if these patients could have gotten clinic appointments more promptly, but most hospital clinics are not set up to serve a large walk-in population.

Same-day appointments usually are not possible at Kings County Hospital, and some clinics may require appointments two to three weeks in advance. It takes almost six weeks to get an appointment in the Kings County Hospital breast clinic. Two patients with diabetes mellitus who said their sugar level had "jumped" were in the emergency room because they were afraid to wait for their next regularly scheduled clinic visit. Similarly, a woman who was registered in the hypertension clinic thought her blood pressure had risen, but was unable to get a clinic appointment until the following week. In the interim, she came to the emergency room.

Patients who went to clinics for special problems often used emergency rooms for more general types of illnesses, when the clinic would have been inappropriate.

Respondents who said they relied heavily on clinics tended to be older than those who regularly used emergency rooms. Their average age was in the mid-50s, and almost all of them had chronic conditions that were monitored through the clinics. In contrast, respondents who never used clinics and received most of their health care in emergency rooms were more likely to be in their 20s and 30s, and to have only transitory illnesses.

TABLE V. Reasons Multiple-Source Users Selected Kings County Hospital Emergency Room for Current Illness Episode

Reason	No. of Patients Who Cited Reason*
Cost	19
Quality of doctors and technology	14
Accessibility	13
Poor/ineffective treatment elsewhere	8
Convenience of location	7
Pharmacy available	6

* Most patients listed multiple reasons for choosing the Kings County Hospital emergency room. The reasons cited here were mentioned most frequently.

Discussion

It is often stated that emergency rooms in low income, inner city neighborhoods are clogged with people who have nowhere else to go for primary health care. Yet interviews with people who were using the emergency room at Kings County Hospital for routine health problems suggested that fewer than 25% had no other source of medical care. Haitian immigrants appeared to be disproportionately represented in this category.

More than 75% of the emergency room users also used clinics and private physicians at times, depending on the nature of the illness episode. But most of these multiple-source users reported that after weighing the severity of the problem against such factors as cost, quality of care, accessibility, and so forth, an emergency room was usually best suited to their needs.

On a nationwide basis, most non-urgent patients use an emergency room mainly when their family physician or clinic is not available; that is, they use the ER as a backup. But for 63% of respondents interviewed in the present study, an emergency room was the main source of health care, and a private physician or clinic was the backup.

For many of those interviewed, cost appeared to be the major factor for their heavy reliance on emergency rooms. Even for those who were employed, resources were extremely limited and there was little money available for health care. Private health insurance, for those who had it, did not cover the full cost of ambulatory care outside of an emergency room, and served as an added incentive for ER use.

Almost 40% of the emergency room patients also used private physicians at times. For those without Medicaid or Medicare coverage, such visits were generally prompted by illnesses they considered serious enough or discomforting enough to warrant expenditures of about $40 per visit, payable in full at the time of the consultation. Though these patients did not necessarily consider their private doctors more competent or skillful than the emergency room physicians, they thought they would receive closer, more personalized attention from the former. For these reasons, private care was perceived as "better."

This raises the issue of who most of the "private" doctors are in low income, inner city neighborhoods. In the communities surrounding Kings County Hospital, there are very few community based private physicians, in the traditional meaning of the term. However, there are many small, storefront, Shared Health Facilities, and other practitioners whose incomes are derived largely from Medicaid and Medicare reimbursements. Patients without any coverage must pay out-of-pocket for their services.

A recent study conducted in the South Bronx, one of the lowest income communities in New York City, indicated that virtually all the community based physicians in the area practiced in SHFs.[9] Since there were 58 of these facilities in the area, as well as several hospitals, the study concluded that the population was not medically underserved, as had been designated. However, the quality of the medical care provided by the SHFs was highly questionable.

The Bronx Professional Standards Review Organization reports that the clinical care provided by most physicians in Bronx SHFs is only marginally acceptable, characterized by an almost total lack of comprehensive care, poor follow-up of abnormal laboratory findings, and excessive and inappropriate use of medications.[10]

From the descriptions offered by several of the non-Medicaid patients in the Kings County Hospital emergency room, it appears that the private physicians they consult for possibly serious problems are most likely SHF practitioners or doctors with mainly Medicaid clientele. Medicaid reimbursement rates are very low in comparison with prevailing private fees, and Mitchell and Cromwell[11] argue that "competition for patients drives less qualified physicians into the [low-paying] Medicaid program in disproportionate numbers," thereby perpetuating a two-tiered form of medicine in which the poor receive inferior care.

Many of the doctors whose primary income is from Medicaid reportedly lack hospital affiliations, have fewer credentials, and are less likely to be board certified than community based physicians who see relatively few Medicaid patients or do not accept them at all.[11,12]

Medicaid practitioners are widely used by the poor; in the South Bronx, for example, SHFs are the principal providers of care.[9] But patients without coverage cannot readily afford these or any community based doctors. Hospital clinics are not an adequate substitute because many of them lack flexibility in terms of appointment scheduling, have limited hours, and may offer specialized services rather than general medical care.

The non-Medicaid low income population has very limited options when it comes to health care, despite the apparent availability of practitioners and facilities in inner city neighborhoods. As perceived by the low income patients interviewed at Kings County Hospital, emergency rooms are a rational and appropriate choice for routine health care, in light of the existing alternatives.

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Endourology: An overview of a new subspecialty

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The diagnosis and management of many urologic conditions is in a state of evolution and revolution, with the interventional radiologist and the urologic surgeon combining their expertise to an extent never before imaginable to create the new field of endourology. With the application of vascular access techniques and the concomitant development of high resolution cross-sectional imaging, the field is in a period of remarkable expansion. Invasive radiologic techniques now interface with and have begun to replace many urologic surgical procedures.

The application of these new concepts and techniques has often obviated the need for surgery, and has replaced the traditional approaches to such diverse entities as obstructive uropathy, renal masses, retroperitoneal fluid collections, renovascular hypertension, and the staging of urologic cancer. Interventional uroradiology represents a refinement of fundamental urologic concepts, whereby formal surgery can be reserved for those patients who cannot be managed by less invasive means.

This review is based on approximately 1,000 endourologic procedures performed at the State University of New York Health Science Center at Brooklyn (formerly Downstate Medical Center) over the past four years.

ORIGINS OF THE SUBSPECIALTY

The forerunner of all the endourologic techniques is the percutaneous needle puncture of the kidney. Percutaneous injection of contrast media into the pyelocalyceal system (antegrade pyelography) was first reported by Kapandji in 1949.[1] In 1954, using radiographic measurements, Wickbom achieved controlled placement of a needle into the collecting system.[2]

The focal point of modern interventional uroradiology is the percutaneous nephrostomy, first devised by Goodwin et al in 1955[3] as a natural extension of the then-new technique of antegrade pyelography. Percutaneous nephrostomy was initially envisioned as a means of providing temporary drainage of an obstructed upper urinary tract, particularly in patients too ill to undergo surgical correction of the obstruction. The original indication for the procedure, as cited by Goodwin in 1955,[3] was uncertainty about the functional status of the obstructed kidney. A temporary nephrostomy allowed the kidney to reveal its potential for recovery of function. A three- to five-day period of diversion often made the difference between nephrectomy and urinary tract reconstruction.

Percutaneous nephrostomy has essentially replaced open surgical nephrostomy. Currently, the most common indication for its use is azotemia secondary to ureteral obstruction.[4] Temporary nephrostomy allows time to prepare the patient for surgery, to give chemotherapy or radiation therapy, and to allow edema to subside postsurgically.

PERCUTANEOUS NEPHROSTOMY

The indications for percutaneous nephrostomy are:

1. Temporary or permanent relief of ureteral obstruction
2. Evaluation of the functional renal status after relief of chronic obstruction
3. Relief of acute septic ureteral obstruction (eg, ureteral calculus) to allow antibiotic therapy preparatory to further manipulation
4. Relief of pyonephrosis

Ureteral obstruction may be due to either benign or malignant disease. If definitive relief of the obstruction cannot be effected, the temporary nephrostomy can be converted to a permanent one using percutaneous techniques. When the ureters are obstructed by malignancy, careful thought must precede the decision whether the patient is a candidate for urinary diversion. Considerations include whether the neoplasm is stable and potentially treatable and whether the patient will be able to return home to a useful life. The quality of life the patient can expect after diversion must also be weighed.

Evaluation of the functional status of the dilated urinary tract is also made possible through percutaneous nephrostomy. Excretory urography is of limited value in estimating the urodynamic status of the postrenal transport system. Whitaker has developed a test of urodynamic function based on a standardized percutaneous fluid infu-

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sion into the kidney with simultaneous pressure measurements in the kidney and bladder (the "Whitaker Test"). The procedure allows differentiation between obstructive and nonobstructive ureteral and pelvic dilatation in the chronically dilated upper urinary tract.[5-7] Briefly, at a standard fluid challenge flow rate of 10 ml/min, a differential pressure (between kidney and bladder) below 15 cm water is normal. Obstruction is indicated if the pressure exceeds 15 cm water and there is a progressive rise with continued fluid administration. This test has primary application in the evaluation of persistent or minimally improving dilatation of the pyeloureteral system after corrective surgery for reflux or obstruction.

The usual therapy for a patient presenting with high fever secondary to an obstructed upper urinary tract infection has been either immediate open surgery or, more frequently, the passage of a ureteral catheter in retrograde fashion via a cystoscope. The placement of a percutaneous nephrostomy tube, however, provides more effective drainage. Since there is no need for general anesthesia, the procedure is safer and more comfortable for the patient.

Pyonephrosis is an absolute indication for drainage. The results are gratifying; patients with a septic condition often undergo defervescence and clinically improve within six to 12 hours. Further manipulation, if required, should be deferred until the infection is bacteriologically clear. The frank pus that is present in this condition cannot be effectively drained through a small bore ureteral catheter.

Complications of Percutaneous Nephrostomy

Successful insertion and maintenance of percutaneous nephrostomy, with minimal morbidity and mortality, can be confidently predicted in more than 98% of cases.[8-10] In a recent survey,[11] the mortality rate for percutaneous nephrostomy was 0.2% as compared to 6% for surgical nephrostomy[12,13] (all deaths in the percutaneous group were secondary to hemorrhage in patients with severe coagulopathies). The complication rate was 4%, with hemorrhage being the most serious, but usually self-limited, complication. Transient hematuria for 24 to 48 hours is to be expected. Infection can usually be avoided by administration of preprocedure antibiotics, adherence to strict aseptic technique, avoidance of overdistention of the collection system, prompt reestablishment of drainage if the catheter should become clogged, and good postnephrostomy care.

Urinomas are rare and avoidable if adequate drainage is established when urinary extravasation occurs. Dislodgement of the catheter from the nephrostomy tract is a cause of urinoma formation, but advances in technology have reduced the incidence of this annoying problem.

The only contraindication to percutaneous nephrostomy is a bleeding diathesis.

Expansion of the Field

Percutaneous nephrostomy is no longer solely a diagnostic or therapeutic end in itself, but can be combined with a variety of other procedures. For example, it provides an avenue of access for the dissolution of certain types of renal calculi. In patients with renal and ureteral calculi, percutaneous nephrostomy was once used primarily to relieve obstruction. It now provides a route whereby these calculi can be dissolved, extracted, or disintegrated. Only local anesthesia is required, thus making the approach particularly useful in poor risk or previously operated patients.

Also facilitated is the percutaneous conversion of the nephrostomy to an entirely internal system for relief of otherwise untreatable ureteral obstructions. Percutaneous nephrostomy with internal stenting has minimal morbidity and mortality rates. Open procedures to achieve drainage in patients with cancer, many of whom are septic, malnourished, or overhydrated secondary to chemotherapy or radiation therapy, are associated with a life threatening complication rate of 45–50% due to sepsis, bleeding, prolonged ileus, and inadequate drainage requiring reoperation.[13-15] From 3% to 8% of patients diverted for obstructing malignant disease die as a direct result of the surgical procedure, while in another 2%, surgical complications contribute significantly to the patient's death.[14]

Percutaneous nephrostomy is also a useful adjunct for instilling antibiotic or antifungal agents.[16] In selected cases of fungal infestation, the percutaneous instillation may replace systemic administration.

Percutaneous nephrostomy also facilitates the treatment of certain cases of superficial upper tract urothelial cancer. The treatment of multifocal upper tract urothelial cancer is controversial and may be a vexing problem, particularly in cases where the patient has a solitary functioning kidney. An investigational technique with only anecdotal experience is the irrigation of chemotherapeutic agents, eg, mitomycin, through the percutaneous nephrostomy.

The percutaneous nephrostomy provides an avenue for antegrade visualization (renoureteroscopy) and manipulation of the luminal aspects of the kidney and ureter for:

- urothelial biopsy, brush biopsy, or aspiration cytology
- dilation, incision, or bypass of ureteropelvic, ureteral, and ileo-ureteral anastomotic strictures
- diagnosis and treatment of anastomotic leaks, especially of the uretero-ureteral and ileo-ureteral versions
- mechanical extraction or ultrasonic disintegration of renal and ureteral calculi and foreign bodies
- placement of devices or agents for ureteral occlusion
- extracorporeal shock wave lithotripsy (ESWL)

Before the development of safe percutaneous techniques, access to the ureter could be obtained only by retrograde cytoscopic or open operative methods. Endoscopic insertion of self-retained internal ureteral catheters was first proposed by Zumskind in 1967.[17] Both benign and malignant strictures or obstructions may be treated by placement of a variety of commercially available stents[18-20] affording relief of pain, restoration of function, and continuous internal drainage, thus obviating the need for permanent pyelostomy or nephrostomy with external drainage.

The antegrade percutaneous technique can be most useful in establishing the diagnosis of upper urinary tract carcinoma. Initially, percutaneous techniques permitted brush biopsy or aspiration cytology in cases where the approach via retrograde catheterization and cystoscopy was not possible. Now, however, in addition to these modalities, a formal biopsy can be obtained using newly developed instruments.

The management of various ureteral strictures is usually a difficult problem. Many patients have been fully radiated or have been operated on previously for both malignant and benign disease. Reimplantation or reanastomosis of a ureter in a radiated field is at best hazardous or contraindicated. The dilation, incision, or bypass of ureteropelvic, ureteral, and ileo-ureteral anastomotic strictures can be effected by percutaneous techniques. Even virgin cases of ureteropelvic junction obstruction have been treated by incision of the junction via a percutaneous access.

One of the more difficult surgical challenges, with a high rate of morbidity and mortality, is the reconstruction of the ileo-ureteral junction after the development of an anastomotic stricture. In such a case the surgeon is working in a previously operated field in an area that frequently has poor blood supply and may have been previously radiated. Two patients referred to us had declined formal revision necessitated by progressive hydronephrosis. We offered the percutaneous placement of indwelling stents. These stents are periodically exchanged for new stents on an outpatient basis. Both patients have been followed for more than three years and have shown no further deterioration of their upper tracts. There have been no cases of sepsis. The patients are maintained on low levels of antibiotics. In the case of radiation induced ureteral strictures, our patients have been offered the placement of an indwelling ureteral stent. For technical reasons, the initial passage of the internal stent could not be effected by retrograde passage. This was easily accomplished, however, by percutaneous antegrade technique. After initial dilatation by the indwelling stent for a period of several months, removal of the stent will usually lead to reformation of the stricture. However, after constant dilatation over a period of years, short term follow-up (six months) has not revealed reformation of the stricture, as judged by sonographic evaluation of the kidney.

We have treated anastomotic leaks in transplant patients by the passage of percutaneous stents via the transplanted kidney.

One of the most useful expansions of the percutaneous technique was the development of methods for the mechanical extraction or ultrasonic disintegration of renal and ureteral calculi. Using well defined techniques, the percutaneous nephrostomy access route can be dilated sufficiently to allow the passage of various instruments that allow direct visualization of the calculus. If the stone is small enough, it can be extracted using a forceps technique. If it is larger, an ultrasonic probe can pulverize the stone and automatically suction out the debris. The technique was initially limited to small stones in the renal pelvis, but has now been expanded to include staghorn calculi and ureteral calculi. The success rate for kidney stones is extremely high but is less so for ureteral calculi. In one case, using percutaneous techniques, we removed the distal tip of a plastic feeding tube that remained in the kidney after the surgeon removed the stent he had used to stabilize the formation of an ileo-ureteral anastomosis at the time of cystectomy. Ordinarily, this would have required an open procedure, but the removal was easily effected in this case by percutaneous techniques.

Occasionally, it is necessary to occlude the ureter on a permanent or temporary basis. In certain cases involving stones, it is useful to occlude the ureteropelvic junction to prevent the distal passage of stone fragments while the case is being managed. Temporary proximal ureteral occlusion has been useful in a number of cases for allowing the healing of distal urinary fistulae.

The recent development of extracorporeal shock wave lithotripsy (ESWL) has been a dramatic and radical departure from prior methods of therapy for renal calculi. ESWL does not replace the percutaneous renal stone techniques, but rather enhances their usefulness. At least 15% of cases suitable for ESWL require adjunctive percutaneous renal or ureteral stone manipulation.

The most common serious complications of endourologic techniques for nephrostolithotomy are hemorrhage, sepsis, and urinary extravasation. Significant hemorrhage is rare, but some postintervention hematuria is to be expected. In our first 100 cases, only one patient required transfusion, and no patients required operative intervention for hematuria or hemorrhage.

Bacteremia and sepsis are always threats in patients with calculous urinary tract obstruction, and it is essential to render the urinary tract sterile prior to stone removal. Often this can be accomplished with the decompression afforded by a percutaneous nephrostomy performed 24–48 hours earlier, along with appropriate antimicrobial therapy.

Urinary extravasation usually results from perforations occurring during wire passage, tract dilatation, or instrumentation. If the collecting system is drained adequately following the procedure, most will heal without complication.

Retroperitoneal Abscesses

We have treated 35 patients with a variety of perinephric, retroperitoneal, and pelvic abscesses. (They are the subject of a separate paper.) The utilization of interventional techniques has markedly improved the treatment of this disease. This entity is not infrequently encountered in the practice of contemporary urology, having been cited as being responsible for one in 600 hospital admissions on one urology service.[12] It represents an emergent problem of insidious onset which if left untreated results in mortality in virtually 100% of cases. In the past, prognosis was grave because diagnosis and localization were difficult. Even with treatment, mortality rates as high as 45% have been reported.[22,23]

Retroperitoneal abscesses can occur as a complication of trauma, infection, or surgery on the genitourinary or gastrointestinal tracts. Compartmental boundaries within the retroperitoneal space and routes of fluid accumulation are the main factors governing the location and progression of the abscess.

The retroperitoneum is divided into four major spaces: The anterior pararenal, the perirenal, the posterior para-

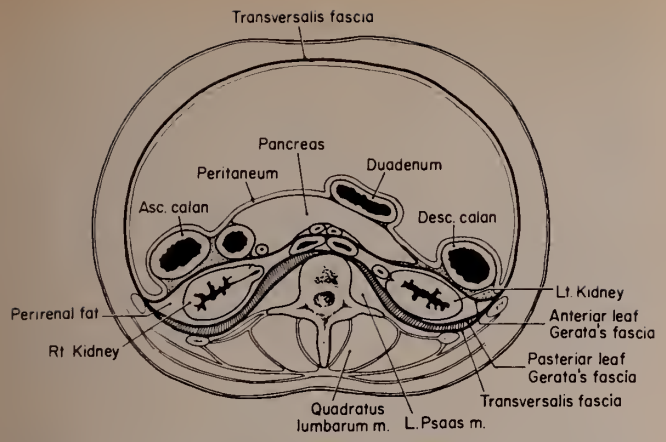

FIGURE 1. An axial section at the level of the pancreas defines the anterior and posterior pararenal spaces. The anterior space between the posterior peritoneum and anterior Gerota's fascia (stippled area) contains the duodenum, pancreas, and ascending and descending colon. The posterior pararenal space (cross-hatched area) between the posterior leaf of Gerot's fascia and the transversalis fascia contains primarily fat. The perirenal space is between the anterior and posterior leaf of Gerota's fascia.

renal, and the retrofascial. Accumulations in the anterior pararenal space include pancreatic abscesses and a variety of paraduodenal and paracolic collections. Perirenal abscesses are most often due to primary renal inflammatory processes. Abscesses of the posterior pararenal space are most often gastrointestinal in origin. The most common retrofascial space collection is the psoas abscess. The perirenal space is closed above but communicates freely with the pelvic retroperitoneal space; the psoas tract represents an unimpeded avenue from mediastinum to thigh (Figs 1 and 2).

Traditional management of these collections has been open surgical incision and drainage. Ultrasonographic

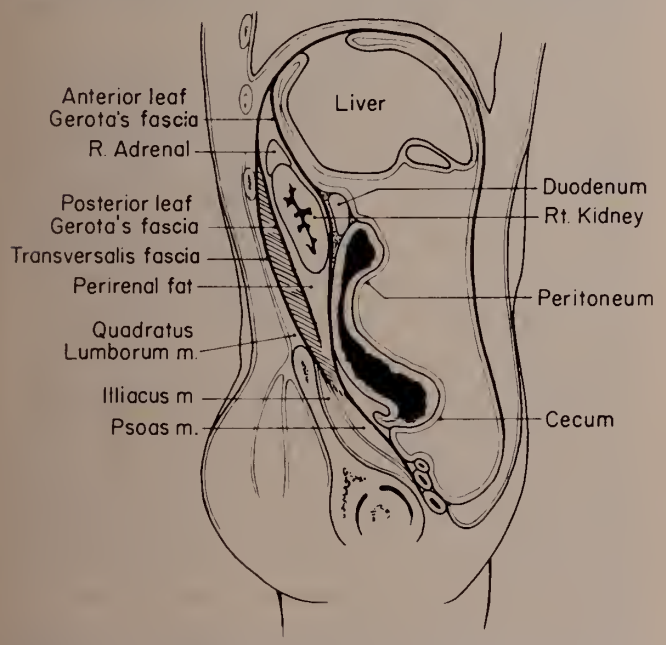

FIGURE 2. A sagittal section through the right kidney also shows the relationship of the anterior and posterior pararenal spaces to the kidney and perinephric space as well as the potential pathway from diaphragm to hip via the psoas muscle. Note that the anterior and posterior pararenal spaces communicate inferiorly.

and computed tomography (CT) guided percutaneous drainage has eliminated the need for surgery in many cases. At our institution, 31 of 35 retroperitoneal abscesses of varied size and diverse etiology have been drained successfully.

Using CT, ultrasonography, and fluoroscopy, safe routes of percutaneous access can be planned, diagnostic aspiration performed, indwelling catheters introduced, and pus evacuated.

Multiloculation of the collection is not a contraindication to drainage and can be overcome with the use of multiple catheters. Even abscesses with fistulae can be successfully managed.

Percutaneous retroperitoneal abscess drainage strictly adheres to established surgical principles by providing decompression, evacuation, and continuous drainage of the abscess cavity. It allows the gentle manipulation of the abscess in order to minimize spillage, hematogenous spread, and subsequent sepsis. Dependent drainage, noncontamination of the peritoneal cavity utilizing an extraperitoneal approach, closed irrigation, sump catheters, and gradual catheter withdrawal to allow healing by secondary intention are all utilized. The technique may be highly successful in critically ill patients for whom surgery is impossible. Percutaneous drainage is a viable alternative that we consider the treatment of choice in the management of the retroperitoneal abscess.

Vascular Techniques

The forerunner of current vascular techniques was the diagnostic renal angiogram. In 1964, Dotter and Judkins introduced a coaxial catheter system for dilatation of atherosclerotic narrowings of the iliac and femoral arteries.[24] The technique was refined by Gruntzig, with the introduction of polyvinyl balloon catheters.[25]

Five percent of the nation's 23 million hypertensive persons have renovascular hypertension,[26] thus there are more than one million people in this country with potentially curable disease.

Numerous surgical revascularization techniques have been employed, resulting in fair cure rates, but associated with an operative mortality rate of 1% to 6% and significant operative morbidity.[27]

Percutaneous transluminal angioplasty (PTA) of a stenotic renal artery segment using a concentrically expanding balloon results in an intimal-medial fracture, with subsequent neoendothelialization and healing effecting a patent lumen. Fibromuscular dysplasia (FMD) appears to be the lesion most amenable to PTA. Cure or improvement can be expected in greater than 95% of cases.[28,29]

Atherosclerotic lesions are inherently more resistant to dilatation than FMD. Although atherosclerosis is progressive, short term results are encouraging, with cure rates of 40–80% reported[26] depending on whether there is intrinsic renal artery disease or aortic disease encroaching on a renal artery. Bilateral renal artery stenosis responds less well than unilateral involvement.

Other treatable lesions are those associated with neurofibromatosis, Takayasu's arteritis, external congenital bands, and postradiation fibrosis. A high success rate has been achieved with stenotic renal allografts.[30]

Vascular Embolization

Therapeutic renal artery embolization has also become a part of interventional uroradiology. A number of materials have been utilized as therapeutic embolic agents, including autologous clot, absorbable gelatin sponge (Gelfoam), steel coils, alcohol, sclerosing agents, nonabsorbable sponge, and cyanoacrylate cement.

Transcatheter embolization of renal carcinoma may decrease operating time and reduce blood loss. In our practice, we restrict embolization to large, bulky tumors. Embolization has also been of benefit in cases of uncontrollable paraneoplastic hypercalcemia.[31] The course of metastatic disease may improve following devascularization of the primary tumor.[32] Other indications for embolization include uncontrollable proteinuria associated with the nephrotic syndrome[33] and uncontrollable hypertension.[34]

Superselective renal embolization is utilized in cases of localized congenital arteriovenous malformations,[35] arteriovenous fistulae subsequent to renal biopsy or trauma,[36] localized renal tumors in a solitary kidney,[37] and intrarenal aneurysms.[38] Complications include embolization, renal infarction, transient elevation of BUN, and renal artery perforation.

Transcatheter venous embolization of varicoceles has gained popularity in recent years, since open surgery is avoided.[39] Indications for varicocele obliteration include infertility, exceptionally large size, and pain. Successful embolization has been reported using detachable balloons, polyvinyl foam, coils, and sclerotherapy.[39] It is our opinion that this technique carries with it too high a failure rate because it does not allow for obliteration of the perforating veins that penetrate the posterior wall of the inguinal canal. Therefore we do not advise it for our patients.

Miscellaneous Aspects

Endourology has simplified the approach to the renal mass in selected patients with documented metastatic disease. If positive, thin needle aspiration biopsy may establish the diagnosis, thus avoiding surgical intervention for purely diagnostic purposes.

Aspiration biopsy of nodes opacified by lymphangiography or, more commonly, delineated by CT, has proven useful in pelvic cancer diagnosis and staging in bladder, prostatic, uterine, and testicular carcinoma.[40] These methods have compared favorably with staging lymphadenectomy.[41]

Conclusions

The percutaneous approach to the urinary tract has rapidly gained acceptance. Endourology represents a fusion of modern urologic and radiologic principles and procedures. Its techniques adhere to hallowed surgical principles but at the same time often obviate the need for formal operation. Procedures utilizing this approach may be carried out under local anesthesia, at a substantially reduced risk to the patient.

Historically, endourologic techniques had been limited to poor risk patients or to those who had already undergone surgical procedures. With the development of high resolution radiologic imaging and guidance techniques, all patients should be offered an initial attempt at percutaneous therapy where it is applicable.

Interventional uroradiology remains a field of tremendous untapped potential. In all institutions where endourology has thrived there has been close cooperation between radiologist and urologist. It is essential that the clinical specialists involved do not regard this young field as a basis for competition. Provision of better patient care is contingent upon the assimilation of endourology into the contemporary urologic armamentarium.

The purpose of this review has been to evoke a general awareness of the new and developing field of endourology, which encompasses a broad spectrum of clinical procedures. These procedures can be applied to a multiplicity of urologic problems without the inherent risk of active surgical intervention and general anesthesia.

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See also pp 510-511 and 527-530.

Current progress in endourology

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The last decade has witnessed the rapid development of a number of urologic procedures directed at the closed management of upper urinary tract disease. The achievements in endourology have been made possible by the design of new instruments capable of providing access to the upper urinary tract and by the innovative efforts of interested urologists. Today, the procedures comprising this growing subspecialty are percutaneous renal and ureteral procedures, including extraction of calculi, dilation or incision of strictures, and diagnosis and treatment of urinary tract tumors; ureteroscopy for diagnostic and therapeutic indications; and extracorporeal lithotripsy of kidney stones.

PERCUTANEOUS STONE REMOVAL

Although percutaneous insertion of nephrostomy tubes has been used to decompress obstructed urinary tracts since the 1950s,[1] the first renal stone removal through a percutaneously created nephrostomy tract was not reported until 1976.[2] Since then, percutaneous stone removal (called nephrostolithotomy or nephrolithotomy) has become the standard approach to virtually all renal, and many ureteral, stones.[3-6]

Percutaneous puncture is preceded, when feasible, by retrograde ipsilateral ureteral catheter insertion, which allows distention of the collecting system and prevents escape of stones into the ureter. The nephrostomy tract may be established preoperatively in a fluoroscopy suite as a separate procedure or, when practical, in the operating suite immediately before tract dilatation and stone extraction. The definitive puncture into the collecting system is made along the posterior axillary line below the 12th rib in most instances but occasionally above the 12th rib if necessitated by a superiorly positioned kidney or the need for access to a particular portion of the collecting system.[7]

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The alternatives to fluoroscopy for location of the renal pelvis and calices are ultrasonography[8,9] and computed tomography.[10] It is also possible to establish the nephrostomy tract retrograde by passage of a needle-tipped guidewire via a ureteral catheter.[11,12]

The percutaneous nephrostomy tract is dilated to accommodate a 34F Teflon sheath, maintains access for introducing the nephroscope into the collecting system, and provides an outflow tract for the large volumes of irrigation fluid used during nephroscopy.

A variety of flexible and rigid nephroscopes are now available. Once the operator has mastered their use, flexible fiberoptic nephroscopes generally permit visual examination of numerous calices that are not reachable by a rigid nephroscope.[13] On the other hand, the rod lens optics and rapid-flow irrigating system of the rigid nephroscopes provide higher resolution of the field image. Most rigid nephroscopes have a direct operating port that allows them to be used with many biopsy and stone-removal instruments. Flexible nephroscopes also accommodate instruments, albeit usually with some sacrifice of flexibility.

Numerous stone-extraction instruments and techniques are available,[3(pp185-237)] and to a large extent, selection of a particular instrument depends on the experience of the surgeon. Triple-pronged forceps provide a firm grasp on large stones but can easily injure the urothelium. Alligator forceps are ideal for grasping stones as large as 5 mm. Stone baskets are particularly useful for stones lodged in the ureter. Stones as large as 1.5 cm in diameter may be extracted intact.

The removal of stones larger than 1.5 cm requires intrarenal fragmentation. The Mauermeyer stone punch is simple to use for renal pelvic stones but it can easily damage the renal pelvis.[14] In 1981, Alken et al described the use of an ultrasound lithotrite through a percutaneous nephrostomy tract.[15] The lithotrite probe effects stone destruction by vibrating at a high frequency while in contact with the calculus. Ultrasound of 20,000 to 27,000 cycles/

sec is generated by a piezoceramic element, and the ultrasound energy is converted into longitudinal and transverse vibrations of a hollow steel acoustical horn which acts as the probe.[16] The central lumen of the acoustical probe is connected to external suction, and constant aspiration of the irrigation fluid serves both to evacuate stone fragments and to cool the probe. The elasticity of the urothelium allows the soft tissue to absorb the vibratory energy with virtually no damage.[17]

The transurethral destruction of bladder stones by electrohydraulic lithotripsy to facilitate their removal has become a routine procedure in urology.[18,19] This technique has also been effective when applied to renal calculi via a percutaneous nephrostomy tract.[20,21] The technique uses electrohydraulic shock waves generated by capacitor discharges at the tip of a coaxial cable. Discharges within 5 mm of soft tissue cause severe damage by heat and the blast effect,[22] and these dangers limit the applicability of electrohydraulic lithotripsy to upper urinary tract stones.

From June 1982 to February 1986, 650 patients have undergone percutaneous extraction of urinary tract calculi at Long Island Jewish Medical Center, and 633 (97.4%) were rendered free of calculi following the procedure. Two hundred seventy-nine patients (43%), most of whom had calculi greater than 1.5 cm in diameter, were treated with ultrasonic lithotripsy. Those patients with exceptionally large stones or stones that resisted ultrasonic fragmentation often required more than one operative session for removal of the entire stone. We recently reported a series of 75 patients with staghorn stones that were treated by percutaneous methods. In 59 patients (79%) only one operative session was required. Fourteen patients (19%) underwent two sessions and only two patients required a third treatment. The overall fragment-free success rate in this series was 86.7%.[23]

The results of percutaneous removal of ureteral calculi in previous reports were disappointing. For example, in an initial series of 200 patients, White and Smith reported a 78% success rate in the percutaneous extraction of ureteral calculi,[24] and Clayman et al were successful in only 70% of the first 44 cases of ureteral and ureteropelvic stones.[25] From July 1984 to February 1985, we attempted to extract 17 ureteral calculi percutaneously, and all but one of the distal ureteral stones were removed percutaneously for a success rate of 94% (Table I). Similarly, Clayman et al succeeded in removing 85% of the 27 ureteral stones seen later in their series. The improvement in the results may be due to technical innovations as well as to increasing experience. For example, the introduction of the peel-away sheath, a flexible Teflon sheath which can be advanced down the ureter to provide ready access to any level with a variety of instruments, has been helpful. Also, Hulbert et al described retrograde flushing of the ureter with carbon dioxide to dislodge impacted stones upward for easier percutaneous extraction.[26]

TABLE I. Percutaneous Extraction of Ureteral Calculi

Location	No. Attempted	No. Extracted	Success Rate (%)
Proximal ureter	14	14	100
Mid-ureter	1	1	100
Distal ureter	2	1	50

The potential complications of percutaneous stone removal include vascular, gastrointestinal, pulmonary, and collecting system injuries.[3(pp313-341),24,25] Despite increasing expertise in the techniques, the frequency of complications has not declined, perhaps because of the increasing difficulty of the cases being attempted; ie, urologists' greater willingness to tackle caliceal and staghorn stones.[27,28]

Chemolysis

In some cases, chemolysis has been combined with percutaneous stone extraction and ultrasonic lithotripsy.[27,28] This technique involves irrigating the collecting system with appropriate solution. Calculi composed of struvite, uric acid, or cystine have responded well to this treatment, whereas calcium oxalate stones have proved resistant to dissolution. Chemolysis has been used to shrink very large stones prior to stone manipulation, to shrink fragments between percutaneous procedures, and to rid the kidney of debris after percutaneous manipulation, especially lithotripsy. The irrigant solution is selected according to the nature of the calculus: Uric acid stones can be dissolved in alkaline solutions such as sodium bicarbonate and tromethamine, while cystine stones, which are also soluble in alkaline solutions, have been dissolved with sodium bicarbonate. For the latter type, results have been further improved by the incorporation of acetylcysteine,[29] D-penicillamine, or Tiopronin.[25] Struvite calculi are soluble in organic acids such as citric acid solutions, to which magnesium is added to reduce irritation. When these solutions are used, serum magnesium levels must be measured frequently and patients clinically monitored for symptoms and signs of hypermagnesemia.[28]

The irrigant may be instilled into the renal pelvis via a nephrostomy tube or a properly positioned ureteral catheter and must be drained effectively to maintain a low pressure system. Alternatives for the drainage of the collecting system include a ureteral catheter, a second nephrostomy tube, or a coaxial nephrostomy tube system. The intrapelvic pressure must be monitored and should be kept below 25 cm of H_2O, as elevated intrapelvic pressure may lead to uptake of the irrigating solution and bacteria or to extravasation. Treatment must be interrupted if the intrapelvic pressure rises above 25 cm H_2O or if the patient suffers severe flank pain.[29,30]

Twenty-four patients (3.7%) at our institution underwent chemolysis in association with percutaneous stone removal. Because of adequate drainage of the system and close observation, no significant complications were encountered, although 16 patients required temporary interruption of the irrigation because of elevated intrapelvic pressure, severe flank pain, or fever.

Endopyelotomy

The percutaneous pyeloplasty, or percutaneous incision and stenting of a stenotic ureteropelvic junction, has been termed "endopyelotomy."[30] The preoperative management is much the same as that for percutaneous stone extraction. The retrograde insertion of a ureteral catheter with its tip proximal to the ureteropelvic junction facili-

tates the opacification of the renal pelvis to establish a percutaneous tract. The ureteral catheter also facilitates negotiation of the ureteropelvic junction. We have found a 6F open-ended ureteral catheter most appropriate for these purposes. By inserting a nephroscope into the renal pelvis, grasping the ureteral catheter or a guidewire inserted through the ureteral catheter, and drawing the ureteral catheter or guidewire out through the nephrostomy tract, percutaneous access across the stenotic ureteropelvic junction is obtained. After inspecting the lateral aspect of the ureteropelvic junction to be certain there are no arterial pulsations, an incision is made there through the mucosa and underlying muscle until the periureteral fat is visualized. The incision is made using an instrument called an optical pyelotome. The ureteropelvic junction is then stented and the stent is left in place for six weeks. We use an 8F or 12F universal stent which can be used to provide internal drainage from the kidney to the bladder or, if necessary, external drainage from the kidney. The universal stent is composed of a silicone rubber which is soft and flexible, allowing the patient to conceal the external portion and to remain in comfort. We have performed 38 endopyelotomies with a success rate of 87% after follow-up periods of as long as two years.[31]

Ureteroscopy

Whereas renal and proximal ureteral stones are readily treated by percutaneous nephroscopy and stone basketing, stones in the distal ureter are usually more difficult to remove from above and may be more amenable to transurethral ureteroscopy. Initial attempts at direct transurethral examination of the ureter were made by introducing pediatric cystoscopes into the ureteral orifice.[32] The development of rigid and flexible ureteroscopes has greatly simplified ureterorenoscopy, which now is applicable in the removal of ureteral stones and the evaluation of upper tract disease.[33,34] Ureteroscopy is facilitated by passage of a guidewire up the ureter.

We have reported a series of 147 ureteroscopic procedures. One hundred nineteen procedures were performed for extraction of distal ureteral stones; 83% of these were successful. Sixty-two percent of ureteroscopic procedures attempted for extraction of mid-ureteral stones were successful.[35]

The complications of ureteroscopic surgery include stricture formation and ureteral laceration and disruption. Small lacerations may be treated by leaving a ureteral catheter in place for two days. Ureteral disruption requires immediate surgical repair; fortunately, this complication is rare. In the hands of an experienced urologist, ureteroscopy is a relatively safe and effective means of treating ureteral calculi and of obtaining ureteral tissue for diagnosis.[36]

Extracorporeal Shock Wave Lithotripsy

In an effort to develop a less invasive treatment for urolithiasis, clinical trials of the extracorporeal shock wave lithotripsy (ESWL) machine were initiated in Germany in 1980. Shock waves of various frequencies, when focused to a single point, deliver significant energy to that point without injuring the tissue through which they pass. The shock waves are generated by an underwater spark which vaporizes the water. The shock waves generated at one focal point of a semiellipsoid propagate spherically, and the energy waves converge at the second focus of the semiellipsoid.[37-39]

A patient with a renal stone is given either general, spinal, or epidural anesthesia, and is placed in the water bath of the ESWL machine. The patient is positioned using a two-dimensional x-ray apparatus so that the renal calculus is located at the second focal point of the ellipsoid. A total of 200 to 2,000 shock waves may be applied in each session in order to fragment the calculus. The stone fragments pass down the ureter and are voided.

Initially, only stones up to 1 cm to 1.5 cm in diameter were accepted for ESWL; more recently, calculi as large as 2.5 cm or even partial staghorn calculi in nondilated collecting systems have been accepted. ESWL has become so popular so quickly that now more than 70 lithotriptor units are operational worldwide and more than 70,000 treatments have been performed.[40]

The initial Food and Drug Administration guidelines for evaluation of ESWL limited it to those patients who had radiodense calculi proximal to the ureteropelvic junction, those patients without infectious stones and without obstruction distal to the stone, and those with stones less than 2.5 cm in diameter. More recently, larger stones and ureteral stones above the bony pelvis have been accepted for ESWL. Radiolucent stones are difficult to treat by ESWL because a stone must be positioned at the objective focal point of the instrument by radiographic localization. This has been managed by filling the collecting system with radiopaque contrast to outline the stone. The contrast may be instilled into the urinary tract via a ureteral catheter or a nephrostomy tube, or may be administered intravenously.

Large struvite or infectious stones were avoided at the outset for fear of septic complications. Proper preoperative antibiotic prophylaxis has prevented most of the severe uroseptic episodes. Another concern when treating large renal stones of staghorn calculi by ESWL is the enormous burden of stone fragments passing down the ureter. The numerous fragments tend to logjam within the ureter, causing obstruction in what is termed a "steinstrasse" effect. This may require another procedure to clear the obstruction and is often amenable to ureteroscopic management.

The stone-free success rate of ESWL varies depending on the position, configuration, and composition of the stone. The ESWL may render 91–96% of patients with a single caliceal stone free of fragments depending on whether the calculus is located in a lower, middle, or upper calix.[41] When multiple caliceal stones are present the overall success rate is 51%, and if the stone burden reaches 5 cm, only 30% of patients will be made stone-free by ESWL.[41]

Various combinations of percutaneous manipulation and ESWL have been attempted to improve the treatment of large partial and complete staghorn calculi. A recent report by Kahnoski et al concluded that ESWL alone for complete staghorn calculi was troublesome. Multiple treatments were required and 75% of patients initially treated by ESWL required either ureteroscopy or percutaneous procedures to clear the fragments.[42] An alterna-

tive approach is to first debulk the stone percutaneously, then use ESWL to fragment the residual stones. Having a nephrostomy tube in place prior to ESWL minimizes urosepsis by providing good drainage and allows more rapid clearance of gravel through the nephrostomy tube.

The present contraindications to ESWL are a pathologic bleeding profile, pregnancy, obstruction distal to the stone, excessive or inadequate height (<120 cm or >200 cm) and obesity (>100 kg).[40] Patients must be able to be supported safely and with adequate mobility while in the bath. Obstruction distal to the stone poses a particular problem since there must be a route for elimination of fragments from the urinary tract.

In addition to the treatment of urolithiasis, endourologic techniques can be used for the management of infundibular narrowing and ureteropelvic junction obstruction.[43] Endopyelotomy may be combined with percutaneous stone extraction in those patients who have calculi proximal to the obstruction. Fungal casts of the renal collecting system have been removed percutaneously followed by systemic and intrarenal treatment with amphotericin. Also, tumors of the renal pelvis have been resected percutaneously, and it is hoped that this may prove a useful alternative to nephrectomy and dialysis for the management of patients with transitional cell carcinoma in a solitary kidney.[44] In the past five years the treatment of urinary tract stones as well as various other urologic diseases has been drastically altered by endourologic techniques. In the near future we will continue to see the changes that endourology will produce.

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See also pp 510–511 and 522–527.

Hemophilus influenzae and *Streptococcus viridans* endocarditis in an intravenous drug abuser

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Endocarditis caused by *Hemophilus* species is uncommon, accounting for fewer than 1% of endocarditis cases reported in earlier series.[1-3] More recently, Geraci et al[4] have reported a higher incidence (approximately 5%), possibly as a result of improved microbiologic techniques. Endocarditis caused by *Hemophilus parainfluenzae*, *Hemophilus paraphrophilus*, and *Hemophilus aphrophilus* predominate, with only nine documented cases of endocarditis due to *Hemophilus influenzae* described to date in adults.[5-11] Of these, six occurred prior to 1965. To our knowledge, no case of *Hemophilus influenzae* endocarditis has been described among intravenous drug abusers. We describe the successful treatment of a patient with *Hemophilus influenzae* endocarditis involving the tricuspid valve in an intravenous drug abuser.

CASE REPORT

A 44-year-old man with a history of intravenous drug abuse was admitted to the hospital for treatment of fever and chills of one week's duration.

Three years prior to admission, the patient was hospitalized for presumed pneumococcal pneumonia. Blood cultures were negative, and an echocardiogram revealed normal valves. There was no audible murmur during that hospital stay. He was treated with penicillin with no complications and he was discharged from the hospital. Despite continued intravenous drug abuse for three years, the patient remained in good health until one week prior to the current admission, when fever, chills, myalgias, pleuritic chest pain, and cough productive of blood-tinged yellowish sputum developed. Intermittent dysuria and hematuria were noted several days before admission, as well as headache, nausea, and progressive shortness of breath. One day prior to admission, the patient took three 250-mg tablets of erythromycin. He came to the emergency room because of persistent fever, chills, and shortness of breath.

The patient had a 30-pack/year history of cigarette smoking and a 15-year history of alcohol abuse and intravenous drug abuse, especially cocaine.

On physical examination, the patient appeared to be a thin, well developed man, with diaphoresis and in mild respiratory distress. His blood pressure was 98/70 mm Hg in the supine position and 90/58 mm Hg standing. His heart rate was 120/min and regular; respiratory rate, 22/min; and oral temperature, 38°C. Decreased skin turgor was present, but there was no rash, icterus, splinter hemorrhages, Osler's nodes, petechiae, or Janeway lesions. The pupils were small, equally round, and reactive. No Roth's spots or hemorrhages were seen on funduscopic examination. Poor dentition and oral cavity hygiene were noted. A 2 cm hard, movable, nontender posterior cervical lymph node and several 2–3 cm right axillary nodes were palpable. Neither jugular venous distention nor hepatojugular reflux were noted. A 2/6 holosystolic murmur was heard best at the left lower sternal border, radiating to the apex, but not to the axilla. Diffuse inspiratory and expiratory wheezes were heard. Tenderness was noted in the right upper quadrant of the abdomen without guarding or rebound, but no abdominal masses were felt. The liver was measured at 10 cm in length on percussion; the spleen was not palpable. Numerous needle marks over both arms were noted.

Laboratory studies revealed a white blood cell count of 9,600/mm^3 with a differential count of 70% neutrophils, 5% band forms, 24% lymphocytes, and 1% monocytes. The hemoglobin count was 12.2 g/dL; hematocrit, 35.3%; and mean corpuscular volume, 88 μm. The electrolyte levels were within normal limits. The erythrocyte sedimentation rate was 110 mm/h. A chest radiograph was within normal limits, and an electrocardiogram revealed only a sinus tachycardia. Urinalysis showed 6–8 red blood cells, but was otherwise unremarkable.

The patient was started on intravenous nafcillin, 2 g every four hours, and gentamicin, 3 mg/kg/day. Subsequently, three of the six initial blood cultures grew both *Hemophilus influenzae* and *Streptococcus viridans*. Two blood cultures drawn one day later grew only *Hemophilus influenzae*. (Identification of *Hemophilus influenzae* was determined by its requirement of both X and V factors after growing on chocolate agar. Typing of the organism was not done.) Ampicillin, 1 g every four hours, was added to the treatment regimen after the culture results were known. Subsequently, an echocardiogram revealed a 2 cm vegetation on the tricuspid valve. The patient continued to have hectic fevers; therefore, the antibiotic regimen was changed four days later to intravenous ampicillin, 2 g every four hours, and streptomycin, 1 g intramuscularly daily. Ampicillin therapy was continued for six weeks, and streptomycin therapy for two weeks. No further blood cultures grew *Hemophilus influenzae*.

The hospital course was complicated by persistent *Streptococcus viridans* bacteremia and septic pulmonary emboli. Two weeks after admission, a dental procedure involving removal of a loose tooth was performed. A repeat echocardiogram five weeks after admission showed no change in the size of the vegetation, and the patient remained afebrile without evidence of congestive heart failure or neurologic complications. The murmur was unchanged throughout his hospital stay. Initially, the *Streptococcus viridans* was sensitive to ampicillin, however, both blood cultures drawn one week after the dental procedure grew organisms resistant to ampicillin. The infection responded to vancomycin and gentamicin, and the patient was discharged without symptoms on the 60th hospital day.

DISCUSSION

Members of the genus *Hemophilus* are fastidious gram-negative coccoba-

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cillary to rod-shaped microorganisms which may be filamentous or may exhibit marked pleomorphism.[12] The speciation of *Hemophilus* has been well described.[12] These organisms are normal inhabitants of the nasopharynx and oropharynx; these sites are probably the usual portals of entry of *Hemophilus* into the blood stream.

There is limited previous experience with *Hemophilus influenzae* endocarditis (Table I).[4-11,13-16] Only 13 well documented cases have been previously reported in the literature, including four in the pediatric age group. Eleven of 13 individuals had lesions involving the mitral or aortic valves, and in approximately 50% there was a known history of underlying valvular disease. There was rarely an obvious source of bacteremia. Of the 13 cases, six of the patients died; two of these were treated prior to 1951 and probably received inadequate antimicrobial therapy. No major embolic phenomena were reported. Although treatment with streptomycin and/or ampicillin was consistently effective in eliminating the infection and yielding clinical improvement, valvular destruction complicated two cases.

This report represents the first reported case known to the authors of *Hemophilus influenzae* endocarditis in an intravenous drug abuser and only the third case of *Hemophilus influenzae* endocarditis involving the tricuspid valve. The patient had no other source of infection. The source of bacteremia was probably either contaminated needles or the oral cavity, especially in view of the patient's poor dentition. The patient had no detectable valvular disease two years prior to admission. This is consistent with 50% of the reported cases in which preexisting valvular disease was absent. However, this patient had a polymicrobial infection, and it is possible that previous valvular damage secondary to *Streptococcus viridans* infection provided a nidus for additional infection with *Hemophilus influenzae*. Previous reviews have reported polymicrobial infections in 11% of *Hemophilus* endocarditis infections, usually with a combination of *Hemophilus parainfluenzae* and *Streptococcus viridans*.[17]

Hemophilus influenzae is a rare cause of endocarditis. It usually presents as a subacute illness with no obvious source of bacteremia. Apparently, normal valves can be affected, and the organism has the ability to cause significant valvular damage. However, major embolic phenomena are rare. Polymicrobial infection, especially with *Streptococcus viridans*, is also common. The treatment of *Hemophilus influenzae* infection with ampicillin alone or in combination with an aminoglycoside is usually effective.[4] At present, experience with treatment of ampicillin resistant *Hemophilus influenzae* endocarditis is limited. Cardiac surgery may be required in instances of severe valvular damage.[15]

We recommend treatment of *Hemophilus influenzae* endocarditis with ampicillin, 2 g every four hours, if the organism is sensitive to this antibiotic. Treatment should continue for six weeks. According to data presented by Geraci et al,[4] even three weeks of drug therapy may be sufficient. Blood cultures must be checked throughout therapy and after completion of the antibiotic regimen. There is insufficient data from the literature to evaluate the use of an added aminoglycoside, but one could postulate that earlier defervescence may be achieved through synergy. There have been no reports to date of ampicillin resistant *Hemophilus influenzae* in cases of endocarditis. Since *Hemophilus* endocarditis often occurs in the setting of a polymicrobial infection, careful attention should be paid to all blood culture results, and additional antibiotics should be administered as indicated.

TABLE I. Reported Cases of *Hemophilus Influenzae* Endocarditis*

Reference	Age (yr)/ Sex	Valve	Therapy	Outcome	Underlying Valvular Disease	Source of Bacteremia
8	19/M	Aortic Mitral	Sulfadiazine	Died	Bicuspid Aortic valve	Sinusitis
6	17/F	Tricusp	Penicillin Sulfadiazine	Died	Rheumatic (mitral)	None
5	25/M	Aortic Mitral?	Penicillin Streptomycin	Survived	Rheumatic	None
5	32/F	Mitral Aortic	Penicillin Streptomycin	Survived	Rheumatic	None
7	37/M	Mitral Aortic	Streptomycin	Survived	Rheumatic	None
4	25/F	Mitral	Pencillin Streptomycin Tetracycline	Survived	None	None
10	48/M	Starr Edwards Mitral	Ampicillin	Died	Rheumatic	Bronchitis
9	79/F	Aortic	Ampicillin Chloramphenicol Carbenicillin	Survived	None	Meningitis
11	57/F	Mitral	Penicillin Streptomycin Ampicillin	Died	None	None
13	1/M	Tricuspid Mitral	Not reported	Died	None	Meningitis?
14	1/M	Mitral	Ampicillin Chloramphenicol	Died	None	Meningitis?
16	3/F	Pulmonic	Ampicillin Gentamicin	Survived	Coronary heart disease	None
15	2/F	Mitral	Ampicillin Gentamicin Cefamandole	Survived (valve replacement)	None	Otitis?

* There are four additional cases included in a literature review by Johnson et al believed to be *Hemophilus influenzae* because of requirement for both X and V factors. In reviewing the specific cases, however, there is no actual documentation of this fact.

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See also pp 511–512.

Lymphangioleiomyomatosis: Treatment with hormonal manipulation

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Lymphangioleiomyomatosis is a rare disease affecting women of child-bearing age that is characterized by hyperplasia of smooth muscle lining the lymphatics of the thorax and abdomen. These pathological changes lead to progressive dyspnea, pneumothoraces, and chylous pleural effusions. The disorder was first described by Cornog and Enterline[1] in 1966; fewer than 80 cases are documented in the medical literature. The following report describes the development of chylous ascites and chyloptysis, two less frequent manifestations of this disorder, and an apparent response to hormonal manipulation with medroxyprogesterone and tamoxifen. In addition, the results of hormonal manipulation in this disease are summarized.

CASE REPORT

The patient was a 45-year-old woman who had a 20-pack/year history of cigarette smoking and had had exertional dyspnea and productive cough for seven years. In 1972, a chest radiograph revealed a diffuse lung lesion; no biopsy was performed at that time.

Ten years later, the patient was hospitalized for the first time with shortness of breath caused by a left-sided pneumothorax. A chest radiograph at that time revealed a diffuse lung lesion and flattening of the hemidiaphragms, in addition to a left-sided pneumothorax (Fig 1). Besides showing signs of a left-sided pneumothorax, physical examination revealed bibasilar mid and late inspiratory rales. A chest tube was inserted, and approximately 1,500 mL of chylous fluid drained from the left hemithorax. Pulmonary function studies done ten days after removal of the chest tube showed a severe obstructive ventilatory defect, significant air trapping, marked hypoxemia, and a severely reduced steady state diffusion capacity. These test results were dramatically reduced when compared to a 1978 study (Table I).

FIGURE 1. Chest film taken on admission showing left-sided pneumothorax and pleural effusion. Diffuse interstitial infiltrates are present in right lung fields.

Later in the patient's hospital stay, an open lung biopsy was performed. Examination of the specimens revealed multiple cystic areas involving the respiratory bronchioles and ducts as well as widespread proliferation of the smooth muscle of the alveolar walls and blood vessels (Fig 2). On the basis of the clinical presentation, chest film, pulmonary function tests, and open lung biopsy, a diagnosis of lymphangioleiomyomatosis was made. The patient was initially treated with medroxyprogesterone, 400 mg intramuscularly twice monthly. During the next several months, her exercise tolerance improved as did her flow rates and oxygen tension (measured February 1983).

A right-sided pneumothorax with a persistent air leak subsequently developed, requiring a right pleural decortication procedure. Following this, chylous ascites and severe hypoxemia that responded poorly to oxygen therapy (Table I) developed (November 1983), and tamoxifen, 20 mg daily, was added to the twice-monthly medroxyprogesterone therapy. Although the patient was severely limited by exertional dyspnea, the arterial oxygen tension improved on a 50% O_2 Venturi mask from the low 60s (prior to tamoxifen) to 86 mm Hg.

In March 1984, the patient's cough became productive of large amounts of milky white sputum, which stained positive for neutral fats. Coincident with this chyloptysis, marked lymphopenia developed, with a total lymphocyte count of 800 cells/mm^3. Fiberoptic bronchoscopy failed to reveal evidence of a broncholymphatic fistula. More severe chest congestion and refractory hypoxemia developed, and several days later the patient suffered ventilatory failure and died.

Autopsy revealed pulmonary fibrosis with diffuse honeycombing and interstitial proliferation of smooth muscle throughout the lung. Although mediastinal and hilar lymph

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TABLE I. Spirometry and Arterial Blood Gases

Date	Forced Expiratory Volume (L)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)
3/30/78	3.24 (104)*	80	31
11/15/82†	0.82 (29)	50	31
2/2/83	1.02 (33)	64	27
5/4/83	1.31 (45)	61	24
11/18/83††	—	67§	22
3/4/84	—	86§	30

* Numbers in parentheses refer to percent of predicted value.
† Open lung biopsy performed and medroxyprogesterone therapy initiated.
†† Tamoxifen therapy initiated.
§ On 50% Venturi mask.

nodes were not abnormal, the retroperitoneal lymph nodes surrounding the inferior vena cava and common iliac veins were enlarged and almost completely replaced by bundles of hyperplastic smooth muscle tissue. No broncholymphatic fistula was seen. Unfortunately, hormonal receptor status was not determined.

Discussion

Lymphangioleiomyomatosis is a rare disease affecting women of child-bearing age that produces a characteristic triad of recurrent pneumothorax, chylothorax, and hemoptysis.[2] Chylous ascites can be present without overt pulmonary involvement.[3] Less frequently, chyluria[4] and chyloptysis[2] are seen. The pathologic hallmark is hyperplasia of the smooth muscle lining the pulmonary lymphatics and, to a lesser degree, the bronchioles, arterioles, and venules.

Severe dyspnea and spontaneous pneumothorax are thought to be caused by the impingement from the abnormal muscle on the lumina of bronchioles, leading to progressive airflow obstruction. Hemoptysis occurs as a result of vascular obstruction and hemorrhage, whereas chylothorax and chyloptysis result from the rupture of lymphangitic cysts. The incidence of hemoptysis and chylous pleural effusions is approximately 40% and 70%, respectively.[2]

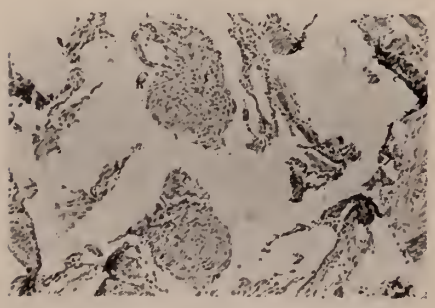

FIGURE 2. Photomicrograph showing nodular proliferation of smooth muscle contiguous to pulmonary lymphatics (hematoxylin-eosin stain, original magnification × 110).

Pulmonary parenchymal abnormalities seen on chest radiographs, reportedly present in 26 of 32 cases,[5] are believed to occur relatively late in the course of the disease. The characteristic finding is that of increased lung volume despite a diffuse infiltrating lung lesion. Initially, a delicate reticulonodular pattern resulting from smooth muscle hypertrophy is seen, while later in the disease a coarse reticular pattern appears, resulting in part from lymphatic engorgement. As the disease progresses, cystic changes are common, as are pneumothorax and chylothorax.[1,2] There have been reports of a few patients who had chylous effusions but no evidence of parenchymal involvement.[5]

Lymphangioleiomyomatosis produces characteristic pulmonary function abnormalities of both airflow obstruction and restriction.[1,2] Airflow obstruction is recognized by a reduced forced expiratory flow (FEF) (25%–75%), maximum voluntary ventilation (MVV), and forced expiratory volume (FEV) (1%). Restriction is characterized by a reduced total lung capacity. In restrictive disorders, the diffusing capacity of the lung for carbon monoxide (DLCO) is well correlated with the extent of lung volume loss, and in emphysema, the DLCO is usually not less than 40% of the predicted value. In contrast, lymphangioleiomyomatosis causes an extremely low DLCO—usually less than 40% of the predicted value. In the case presented here, the DLCO in November 1982 was 25% of the predicted value. Arterial hypoxemia and hypocapnia are the rule, although hypercapnia is seen in the end stage of the disease.

Until recent years, attention has focused on the management of complications associated with lymphangioleiomyomatosis, rather than on specific therapy for the disorder. Thoracostomy performed via a chest tube, pleurodesis, or pleurectomy have been the standard treatments for recurrent pneumothoraces. Chylous ascites has been treated with dietary fat restrictions and use of medium chain triglycerides with some success.[3] The use of a LeVeen peritoneovenous shunt enabled long term regression of chylous ascites in one patient,[6] while a peritoneal shunt was not helpful in another.[7]

Because lymphangioleiomyomatosis affects women of child-bearing age and because symptoms can be exacerbated during pregnancy or in the postpartum period, hormonal manipulation has been attempted. While results are mixed, hormonal manipulation has received theoretical support from the isolation of hormone receptors in involved tissue.[8,9] The results of hormonal manipulation are summarized in Table II. Bush[10] was the first to try hormonal manipulation, unsuccessfully using androgens in a patient with advanced disease. Kitzsteiner[6] and Banner[11] each reported a case of lymphangioleiomyomatosis treated with oophorectomy; both patients were stabilized by clinical criteria and pulmonary function over a four- and a four-and-a-half-year period, respectively. These results contrast with Kreisman's[12] report of a 48-year-old woman with progressive disease despite bilateral oophorectomy. A 33-year-old woman who had progestin receptors present in lung tissue responded well to therapy with monthly injections of medroxyprogesterone, as shown by improvement in arterial blood gases and exercise tolerance to progesterone.[8] This patient's clinical status worsened when therapy was discontinued, but improved again when medroxyprogesterone was restarted. Anti-estrogen therapy with tamoxifen did not halt disease progression in a patient originally described in Carrington's series.[13]

The patient described in this report had minimal but distinct improvement in exercise capacity and some improvement in oxygen tension in response to tamoxifen, but remained severely limited by exertional dyspnea and required a 50% oxygen Venturi mask for adequate oxygenation.

Most research with steroid receptors has dealt with breast and gynecologic neoplasms. There is a greater likelihood of responsiveness to hormonal manipulation if both estrogen and progesterone receptors are present.[14] Perhaps an analogous situation exists in lymphangioleiomyomatosis. In the patient described by McCarty,[8] the tissue contained progestin receptors, and the

TABLE II. Results of Hormonal Manipulation

Reference	Age at Diagnosis (yr)	Duration of Pulmonary Symptoms (yr)	Forced Expiratory Volume 1 (L)	PO_2* (mm Hg)	Hormone Receptors	Treatment	Response	Comment
10	27	9	—	66	Not done	Tamoxifen, 20 mg daily	No	Also received cyclophosphamide
12	48	2	1.95 (71)†	61	Not done	Bilateral salpingo-oophorectomy at age 47 for leiomyomas	No	
6	23	Recent onset	2.28 (83)	71	Not done	Bilateral salpingo-oophorectomy	Yes	Pulmonary function stable for four years
11	47	19	1.80 (69)	96	Negative on ovary for estrogen	Right oophorectomy at age 28	Probably not	Done to remove cyst
						Left oophorectomy	Yes	Pulmonary function stable for four and a half years
9	32	1	—	61	Negative progestin	Medroxyprogesterone, 400 mg every two weeks	No	Died from respiratory failure four months after treatment
	32	1	—	46	Positive progestin	Bilateral salpingo-oophorectomy	No	
8	33	3	—	69	Positive progestin	Medroxyprogesterone, 400 mg every month	Yes	Pulmonary function worsened off progesterone, improved when put back on
18	36	1–2	—	43	Not done	Medroxyprogesterone, 10 mg every day; Tamoxifen, 20 mg daily	No	Died of respiratory failure
15	27	1–2	—	62	Negative progestin Negative estrogen	Medroxyprogesterone	Yes	Better clinical status, but six hospital stays in following two years
Present case	40	7	2.29 (61)	50	Not done	Medroxyprogesterone, 200 mg every two weeks	Yes	Improved exercise capacity; slightly improved forced expiratory volume 1 and PO_2
	40	7	—	57 (on 50% Venturi mask)	Not done	Tamoxifen, 20 mg daily	Probable	Improved exercise capacity and PO_2
13	31	10	0.88 (29)	38	Not done	Tamoxifen, 20 mg daily	No	Was in cor pulmonale when tamoxifen was started

* Prior to hormonal manipulation on room air.
† Number in parentheses is percent of predicted value.

patient's condition improved with hormonal therapy. Two patients whose tissue did not contain hormone receptors may have responded to hormonal therapy, but one required six hospital visits in the following two years,[15] and the other may have had slowly progressive disease.[11]

If there is an effect of hormonal therapy in lymphangioleiomyomatosis, it is often short-lived, as this case illustrates. Although there are several possible explanations for this lack of sustained effect, the most likely is that the underlying disease is usually far advanced at the time of initiation of therapy. It is also possible that such therapy may cause a progressive decrease in lung tissue receptors, as has been demonstrated in the treatment of breast cancer with tamoxifen.[16,17] Finally, the receptor itself may be comprised of subunits that can combine in ways that result in varying degrees of hormonal responsiveness. Such a condition appears to exist in estrogen receptors in breast tissue.

Though there have been some encouraging results in lymphangioleiomyomatosis with progestational and anti-estrogen agents, the role they play in altering the natural history of the disease remains speculative. As more experience with steroid receptors in lymphangioleiomyomatosis is accrued, the precise role of these agents will become better defined.

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Unilateral hypertrophy of the cervical ligamentum flavum presenting as a pseudotumor

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Thickening of the ligamentum flavum is a common disorder, but focal unilateral hypertrophy is rare. This report presents radiographic findings for a unilateral thickening of the ligamentum flavum, with degenerative bony hypertrophy of the cervical spine. In combination, myelography and metrizamide computed tomographic (CT) scans yielded a preoperative diagnosis of an extradural mass or nodule in the midcervical region. Focal compression and obliteration of the subarachnoid space were noted. A review of the literature focuses on this abnormality of the ligamentum flavum.

Case Report

A 60-year-old man sought treatment for right-sided extremity incoordination, right arm weakness, and parasthesia. There was no prior trauma to the cervical spine. A neurologic examination showed atrophy of the right deltoid and biceps muscles, with decreased vibration and absent pinprick responses in the right upper and lower extremities, bilateral leg paraparesis, and positive Babinski's reflexes—more pronounced on the right than on the left.

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FIGURE 1. Lateral view of a metrizamide cervical myelogram showing compression and obliteration of the subarachnoid space, predominantly along its posterior aspect.

Conventional radiographs of the cervical spine revealed no disc space narrowing, bony sclerosis, hypertrophic spurring, or unusual calcifications within the posterior arch.

A metrizamide cervical myelogram (Fig 1) showed extradural right posterolateral cord compression by a mass effect extending from C3 to C5. A four-hour delayed metrizamide CT scan (Figs 2,3) revealed a stenotic cervical spinal canal with hypertrophic spurring along the vertebral bodies and posterior arches.

Confirming the myelographic findings, this CT study identified an extradural nodular mass along the right posterolateral side of the spinal column at the C4 level. There was also bilateral hypertrophy of the uncinate processes, with associated narrowing of the neural foramina, which was considered responsible for the compression of the bilateral dorsal nerve root. The mass was initially thought to be an extradural benign tumor, such as a meningioma or, less likely (since there was no erosion or widening of the neural intervertebral foramina), a neurofibroma.

FIGURE 2. Metrizamide axial CT scan at the C4 level showing a filling defect of the subarachnoid space along its right posterolateral aspect. Small gas bubble in the anterior subarachnoid space was introduced during myelography.

FIGURE 3. Metrizamide axial CT scan at the C5 level shows no abnormal filling defect or compression of the subarachnoid space.

The patient underwent laminectomy at the C3 to C5 levels. Focal thickening of the ligamentum flavum was observed at the C4 level; this caused unilateral blockage of the flow of cerebrospinal fluid and compression of the spinal cord. Both the dentate ligament and the thickened ligamentum flavum were sectioned around the site of compression. After surgery, the patient's strength gradually increased, although he had residual, but milder, paraparesis of the right arm.

Discussion

The ligamentum flavum consists predominantly of yellow elastic tissue attached to contralateral laminae and articular processes at each vertebral level. It forms the posterior wall of the spinal canal.[1] It also extends longitudinally from the second cervical arch to the first sacral posterior arch, connecting each lamina with the adjacent lamina above or below.

In its normal state, the ligamentum flavum is composed of a vertical array of elastic connective tissue fibers, which are extremely dense and represent the purest elastic tissue in the human body.[2] However, with natural aging or degenerative changes this ligament becomes thicker. This thickening is a result of replacement by fibrotic tissue, increasing collagen content, the addition of ossific or cartilaginous components, hyalinization, increased number of blood vessels, fatty infiltration in perivascular spaces, and fragmentation and splaying of elastic fibrils.[3,4]

Within the normal cervical spine, the ligamentum flavum is generally 1.5 mm in maximal thickness. Yet on neck extension, this ligament bulges anterolaterally and may reduce the diameter of the spinal canal by as much as 30%.[2] Taylor[5] used radiographic evidence to demonstrate this reduction: he injected contrast dye into the cervical spines of cadavers, and demonstrated defects in the dorsal subarachnoid space after neck extension. The resultant compression of the spinal cord or nerve roots may be exacerbated by hypertrophic spurring, disc bulging or herniation, or congenital spinal stenosis.

Pathologic thickening of the ligamentum flavum is most likely to occur in hypermobile spinal segments, primarily the lower lumbar or midcervical levels.[6] In such flexible regions there is continual movement and stimulation, which may result in excessive development of fibrous connective tissue. The pathogenesis of strain and thickening associated with hypermobility is presumably due to trauma or long standing intervertebral disc disease.[3]

However, there are isolated reports of such thickening secondary to syphilitic or tuberculous granulation tissue,[7] necrobiotic nodules or cysts,[8] calcium or ossific deposits that form after trauma or degeneration,[9] uric acid crystals in gout,[10] and calcium pyrophosphate dihydrate (CPPD) crystals in the pseudo-gout syndrome.[11] In other cases,[4,12] the cause of the thickening is uncertain, as there is no history of trauma, spondylosis, or granulomatous disease.

In 1913, Elsberg[13] reported the first case of a thickened ligamentum "subflavum" that compressed a lower lumbar dorsal nerve root after previous trauma and rupture of the ligament. For at least half a century, this abnormality was observed only in the lumbar spine.[3,8] Not until 1978 was the disorder first associated with cervical radiculomyelopathy.[14] Although the thickening is usually bilateral,[1,11] it may be focal in response to localized injury or calcium deposits.[12,15]

The diagnosis of this intraspinal deformity is seldom made from clinical and laboratory results alone. Conventional radiographs or laminograms of the spine may reveal hypertrophic lipping or post-traumatic bony fragments within the ligamentum flavum,[16] but plain roentgenograms are generally insufficient. As early as 1936, myelography was recommended as being of "paramount importance" in the differential diagnosis of cord compression.[15]

Recently, computed axial tomography with serial thin sections and reconstructed images has been used to identify ossification within prominent ligamenta flava of the thoracic spine.[17,18] Another CT study[19] illustrated bilateral thickening of this ligament in the cervical region. However, to our knowledge, the combination of CT scans and myelography in diagnosing unilateral hypertrophy of the ligamentum flavum has not previously been reported.

Roentgenologic analysis is important in the recognition of a thickened ligamentum flavum. A metrizamide myelogram can reveal an extradural posterolateral or posterior indentation of the dural sac, resulting in partial or complete blockage. A complementary CT scan with metrizamide may further help to identify small calcifications within the ligament, and may also reveal the degree of nerve root or cord compression. Axial CT scans also delineate the configuration and size of an enlarged ligament, as well as internal cysts or nodules, if present.

While these radiologic procedures can refine the preoperative differential diagnosis, they may lack complete specificity. A thickened fibrotic ligament can simulate an extradural tumor, a small granulomatous or inflammatory change, or, perhaps, focal pachymeningitis.[4] Surgery and histologic analysis are thus required to yield the final diagnosis.

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Acute onset of diabetes insipidus in a patient with an active vasculitis

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Central diabetes insipidus is an uncommon disease in which a deficiency of antidiuretic hormone (ADH) leads to an inability to produce concentrated urine. Various degrees of ADH deficiency are recognized, including total absence of detectable endogenous hormone secretion. Often the disease occurs spontaneously during the first two decades of life. When a cause is found, it usually involves a hypothalamic disorder that affects ADH synthesis, or a destructive lesion of the posterior pituitary causing retrograde degeneration of secretory neurons from the hypothalamus.[1] We report here a case of central diabetes insipidus that occurred in a young woman suffering from juvenile rheumatoid arthritis and an associated severe vasculitis.

CASE REPORT

The patient, a 20-year-old woman with at least a three-year history of juvenile rheumatoid arthritis, also had hereditary spherocytosis, with associated mild anemia. At the age of 11, band keratopathy was detected by an ophthalmologist. Six years after the diagnosis, pain and swelling of the right knee developed. Later, stiffness developed in the knees, wrists, fingers, ankles, and toes. There was no fever or rash. A diagnosis of juvenile rheumatoid arthritis was made, and the patient was initially treated with high doses of aspirin. Nodules developed at the olecranon bursa. Later, the patient experienced an acute episode of periungual petechiae and skin infarctions, together with stridor secondary to bilateral paralysis of the vocal cords. The paralysis was presumed to be due to vasculitis of the vasa nervorum. This acute episode resolved following therapy with high dose glucocorticoids and penicillamine. Penicillamine therapy, 500 mg daily, was then maintained.

Six months later, necrotic lesions appeared on the patient's thigh that resolved on continued penicillamine therapy. Ulcerations then appeared in the oral mucosa. Penicillamine was discontinued, without improvement of the oral mucosa. Two months after the discontinuation of penicillamine, the patient noted the onset of polyuria and polydipsia. Evaluation by an ophthalmologist at this time revealed keratoconjunctivitis sicca. With the onset of polyuria and polydipsia, the necrotic skin lesions also recurred. A skin biopsy showed leukocytoblastic vasculitis with considerable nuclear dust and many neutrophils in a predominantly pervascular location within the dermis (Figs 1, 2). High dose glucocorticoid therapy was begun. Because of a lack of response, the patient was admitted to the hospital, and penicillamine therapy was reinstituted. The skin lesions rapidly resolved. One week after the initiation of this therapy, a detailed endocrine evaluation was performed.

Routine laboratory values of note included an admission hematocrit of 34% and normal electrolyte levels. Initial hormone studies revealed normal thyroid functions, with a free thyroxine value of 2.2 ng/dL (normal range, 0.8-2.3 ng/dL) and a prolactin level of 24.1 ng/mL (upper limit, 22 ng/mL). Glucocorticoid levels were presumed to be supraphysiologic, since the patient was receiving 30 mg of prednisone during this time. There was a regular menstrual cycle, and normal thirst and temperature regulation.

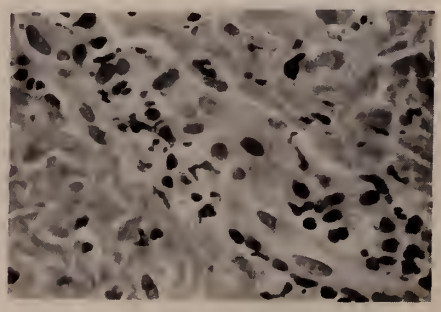

FIGURE 1. Skin biopsy showing a small blood vessel infiltrated by neutrophils and nuclear dust (original magnification × 400).

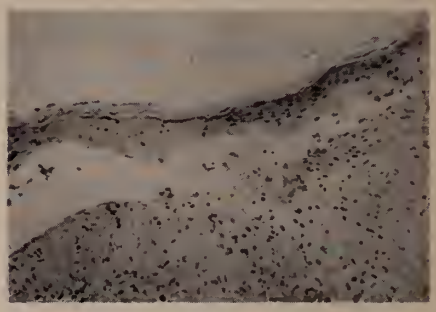

FIGURE 2. Skin biopsy showing subepidermal bulla (original magnification × 100).

A computed tomographic (CT) scan of the brain, with 1.5 mm coronal cuts through the sella turcica and suprasellar region, revealed no evidence of pituitary or hypothalamic disease. One week after admission, a water-deprivation test was begun after the patient had received nothing by mouth since midnight. The Table provides evidence to support the diagnosis of complete central diabetes insipidus.[2] There is no evidence of any endogenous vasopressin release, even after the blood osmolality reached 307 mosm.

The patient was placed on desmopressin acetate, initial dose 0.1 cc intranasally twice a day, with complete amelioration of the polyuria. Six months later, glucocorticoid and penicillamine therapy had been successfully tapered off, and the patient required only 250 mg/day of naproxen for control of arthritic symptoms. At this time, the desmopressin acetate was temporarily discontinued. However, polyuria immediately ensued, with specific gravities of the urine ranging from 1.000 to 1.002.

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TABLE. Water Deprivation Test

	Urine		Blood			
Time	Volume (mL)	Osmolarity (mosm/L)	Osmolarity (mosm/L)	Antidiuretic Hormone* (pg/mL)	Weight (kg)	Medication
0800	Void		298		49.4	
0900	400	108				
1000	300	131	302			
1100	200	168				
1200	200	158	306			
1300	150	221†				
1330	120	178	307	Less than 0.9 (normal, 2–12 if serum osm >290)	47.9	
1335						Aqueous Pitressin (5 U sc)
1400	100	290				
1440	60	637				

* Assay performed at Bioscience.

† Some contamination with blood. All other specimens clear, with no blood. (The patient's normal menstrual flow had ended one day prior to this test.)

Discussion

Diabetes insipidus is a rare disorder. In one third of cases, no cause of the diabetes insipidus is found.[2] The most common known causes of diabetes insipidus are hypothalamic and pituitary tumors, severe head trauma, neurosurgical procedures, and granulomatous diseases.[1,3,4] Rarely, a vasculitic lesion has been demonstrated as a cause of diabetes insipidus. Several occurrences of diabetes insipidus in patients with Wegener's granulomatosis and one occurrence in a patient with thrombotic thrombocytopenic purpura have been described.[5,6]

The patient described here had diabetes insipidus in association with a collagen disease vasculitis. We are unable to document such an association in the literature. Although it is possible that diabetes insipidus developed spontaneously—not in association with the underlying juvenile rheumatoid arthritis—the development of diabetes insipidus during the acute phase of vasculitis makes this unlikely. Drugs cannot be implicated in the development of the diabetes insipidus, since the patient's polyuria began prior to restarting drug therapy for vasculitis and persisted when the only medication being administered was low dose naproxen. In all likelihood, this patient suffered an infarction in her hypothalamus. Definitive proof of such a cause for the diabetes insipidus would require histologic evaluation of hypothalamic tissue.

Whether the patient's hereditary spherocytosis contributed to the development of diabetes insipidus cannot be answered satisfactorily, although it remains an unlikely possibility. This disease of the red blood cells is not associated with parenchymal lesions of the brain or any other organ. However, the mild anemia it induced could have played a role in the development of an infarction of the hypothalamus.

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Plasma cell leukemia with meningeal involvement

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Plasma cell leukemia is a neoplastic proliferation of plasma cells characterized by at least 20% plasmacytosis in the bone marrow and greater than 2,000 plasma cells/mm^3 in the peripheral blood. Plasma cell leukemia can develop de novo or can occur in the end stages of multiple myeloma.

Meningeal involvement in plasma cell dyscrasias is rare. While a few cases of multiple myeloma involving the central nervous system (CNS) have been described, there have been only three reported cases of plasma cell leukemia that resulted in leukemic meningitis.[1–3]

We describe a patient who had plasma cell leukemia of unusually long duration, with meningeal involvement. Early diagnosis resulted in control of the CNS disease and prolonged survival.

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Case Report

A 51-year-old woman sought treatment for weakness and fatigue in November 1983. Lymphadenopathy and hepatosplenomega-

ly were found on physical examination. Laboratory data were remarkable for a white blood cell count of 31,000/mm^3 with 22% plasma cells; hematocrit, 14%; blood urea nitrogen, 80 mg/dL; and creatinine, 10 mg/dL. Serum protein electrophoresis showed a gamma globulin spike with a monoclonal lambda light chain. Bence Jones protein was detected in the urine. A skeletal survey was negative. A bone marrow aspirate contained hypercellular marrow with 80% plasma cells.

A diagnosis of plasma cell leukemia was made, and the patient was treated with cycles of cyclophosphamide, 750 mg/M^2 intravenously, and prednisone, 200 mg/M^2 orally, for five days. She required a brief course of hemodialysis. The creatinine level declined from 11.6 mg/dL to 3.0 mg/dL over a four-week period. After six cycles of therapy, the patient's serum creatinine level was 3.0 mg/dL; hematocrit, 37%; platelet count, 107,000/mm^3; and white blood cell count, 5,200/mm^3 without circulating plasma cells.

Six months later, the patient complained of generalized weakness and fatigue. She had increasing renal failure (creatinine, 5.2 mg/dL) and 27% circulating plasma cells. A bone marrow aspirate was hypercellular, with 100% plasma cells. Intravenous dexamethasone, continuous infusion of vincristine, and adriamycin were administered, with no response.[4] Cycles of cyclophosphamide, 750 mg/M^2 intravenously, adriamycin, 40 mg/M^2 intravenously, vincristine, 1 mg/M^2 intravenously, and prednisone, 200 mg/M^2 orally, for five days every four weeks were started. The peripheral plasmacytosis resolved, and renal function improved.

Ten months after the initial presentation, occipital headaches, projectile vomiting, truncal ataxia with a wide-based gait, and hyperreflexia developed. No abnormal plasma cells were noted on the peripheral smear.

A lumbar puncture revealed an opening pressure of 380 cm water, a protein count of 670 mg/dL, and a glucose level of 87 mg/dL, with 91 cells/mm^3, all plasma cells. Protein electrophoresis of the cerebrospinal fluid (CSF) revealed an increased gamma globulin level of 16.4% (upper limit of normal, 13%). A computed tomographic scan of the head showed a lesion in the left parietal lobe, as well as meningeal enhancement consistent with a plasmacytoma and meningeal inflammation.

A Leroy intraventricular reservoir was set in place, and the patient was given six doses of intrathecal methotrexate, 12 mg/M^2, and systemic chemotherapy with cyclophosphamide, adriamycin, vincristine, and dexamethasone. Cranial irradiation was administered, with a total of 2,400 rads given in 12 treatments.

The patient experienced complete resolution of symptoms after the first dose of dexamethasone and intrathecal methotrexate. The number of plasma cells in the CSF steadily decreased, with complete clearing by the fifth week of therapy. Sixteen weeks later, the patient suffered a peripheral blood relapse and increasing renal insufficiency. She refused further therapy and died of renal failure 18 months after the original diagnosis. An autopsy was not obtained.

Discussion

Leptomeningeal involvement in plasma cell dyscrasias is rare.[5] In this patient, meningeal involvement was suspected on the basis of abnormal neurologic findings consistent with elevated intracranial pressure. Interestingly, there were no "classic" meningeal signs. Cytologic analysis of the spinal fluid revealed plasma cell exclusively, and protein electrophoresis demonstrated the same gamma globulin as in the peripheral blood. Notably, the CSF gamma globulin concentration was higher than that in the serum, suggesting that plasma cells in the CSF were actively secreting immunoglobulin. Treatment with weekly intrathecal methotrexate and whole brain irradiation resulted in control of the CNS disease.

This case is remarkable for the patient's long survival following intensive chemotherapy—distinctly unusual in plasma cell leukemia. Neurological signs developed ten months after the initial presentation. The patient suffered from two simultaneous but independent processes: leptomeningeal involvement and a solitary lesion (plasmacytoma). These findings suggest a hematogenous spread of the disease, as opposed to spread by direct extension from involved bones.

A diagnosis of plasma cell leukemia meningitis was made prior to death in only two of the three such cases reported in the literature. In a patient with IgD plasma cell leukemia, diffuse involvement of the meninges by plasma cells was found at autopsy.[1] In addition, perivascular cuffs of plasma cells were noted around the cerebral blood vessels, a finding seen in acute leukemia. No neurological symptoms or findings were reported in the case record.

Another case involves a 49-year-old man with IgG plasma cell leukemia in whom grand mal seizures, meningeal signs, and a change of mental status developed.[2] A lumbar puncture revealed a markedly elevated protein level, a normal glucose level, and numerous plasma cells. Despite whole brain irradiation and intrathecal methotrexate therapy, the patient died two weeks later.

A third patient with plasma cell leukemia and meningeal involvement had palsy of the seventh and twelfth cranial nerves.[3] Therapy with intrathecal methotrexate and whole brain irradiation was unsuccessful, and the patient died shortly thereafter.

The presentation of plasma cell leukemia with meningeal involvement can vary from that of "classic" meningitis to disease with nerve palsies and paresis, to signs suggestive of increased intracranial pressure. In all cases, CSF analysis revealed a high protein concentration with a normal glucose level and positive cytologic findings.

Meningeal involvement has also been described in patients with multiple myeloma.[5-9] Meningeal involvement seems to be more common in patients with IgD multiple myeloma, especially IgD-1, although it has been described in association with other myeloma paraproteins. Patients in whom plasma cells are detectable in the peripheral smear, albeit in quantities insufficient for the diagnosis of plasma cell leukemia, seem to be at increased risk for CNS involvement. The prognosis for each of these patients appears to depend on the ability to control the systemic disease. Treatment of the meningeal process seems to be warranted and, as in the patient reported here, can produce a long term response.

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Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

Medical record ownership in a professional medical corporation

TO THE EDITOR: A question frequently asked by physicians who were formerly employed by professional service corporations is whether the physician or the professional service corporation owns the medical records that were prepared by the physician during his or her employment. Physicians usually think they should have ownership rights to the records of those patients for whom they were the primary treating physician.

One recently decided opinion, *Parsley v Associates in Internal Medicine*,[1] holds that unless provided otherwise by contract, physicians employed by professional service corporations have no ownership rights to the medical records that they produce during the course of their employment. In rendering its decision, the court applied general principles of corporate law: Since the physician employee is the agent of the corporation, records produced by the agent in the course of the performance of his duties are the property of the corporation.

The court in *Parsley* distinguished the case from *Damsker v Hague*,[2] which involved an attempt by a physician to obtain medical records from the shared health facility in which his office was formerly located. In *Damsker*, the shared health facility was directed by the court to make available to the physician, at cost and in an expeditious manner, copies of the medical records of patients for whom he was the primary or treating physician. In contrast to a professional service corporation, which may render professional services through its professional staff,[3] a shared health facility, as an entity, cannot render professional services or establish a physician-patient relationship. A shared health facility is required by law to "assign an individual and clearly identified practitioner to all patients."[4]

While a physician employee of a professional service corporation may not have ownership rights to the medical records that he produces during the course of his employment, this may be altered by contract. A physician may wish to insert a clause in his contract with a professional service corporation that holds that upon his leaving employment, he may obtain, at cost, copies of medical records where he was the primary or treating physician.

Even without the right of ownership to medical records, all physicians have access to copies of medical records as provided by section 17 of the New York State Public Health Law. Pursuant to this law, upon the written request of a patient, a physician or hospital must transfer a copy of the records relating to the medical treatment of the patient to any other physician or hospital. Reasonable costs incurred in transferring the copies may be charged to the patient.

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1. *Parsley v Associates in Internal Medicine*, 484 NYS 2d 485 (Sup Ct, Broome Cty, 1985).
2. *Damsker v Hague*, 461 NYS 2d 27 (Sup Ct, App Div, 1st Dept, 1983)
3. New York State Business Corporation Law §1504(c).
4. New York State Public Health Law §4710-(1)(e).

Fungemia due to *Hansenula anomala*

TO THE EDITOR: Ascomycetous yeast infections in humans are extremely rare. During the 1950s and 1960s, various authors[1-3] described some of the species of this class, including *Hansenula anomala*, as opportunistic pathogens. In 1980, McGinnis et al[4] described a child with granulomatous disease in whom an infection of the mediastinal lymph nodes developed due to *Hansenula polymorpha*.

We recently treated a patient with fungemia which was found to be due to *Hansenula anomala*. To our knowledge, ascomycetous yeast generally, and *H anomala* in particular, have not been reported in human blood.

Case Report. A 57-year-old man was transferred from a skilled nursing facility to the hospital because of a temperature rise to 101°F. The patient was obese and had suffered from multiple sclerosis and quadriplegia since 1965. He was found to have a urinary tract infection due to *Pseudomonas aeruginosa*. Respiratory difficulties and signs of hypoxia also developed. The patient received ampicillin and amikacin and was placed on a Bantam respirator. He also received bronchodilator therapy to mobilize thick secretions. The patient refused both a tracheostomy and intubation.

In the following months, decubitus ulcers developed, and the patient suffered several episodes of pneumonitis. A sputum culture was positive for *P aeruginosa* and yeast-like microorganisms. The only other pertinent laboratory data were a blood sugar level of 147 mg/dL and a white blood cell count of 14,700/μL. He became weak and diaphoretic. At this stage, a blood culture was done by using a Bactec 460 (Johnston Laboratories, Cockeysville, Md), which revealed a yeast-like organism that was identified as *Hansenula anomala*. A second blood culture done three days later showed the same organism. A ten-day course of intravenous amphotericin B cleared the infection, and the patient's condition became stable.

Discussion. There are few reports of human infections due to organisms of the genus *Hansenula*.[3,4] The various species of this genus are usually found in plants, soil, fruits, and also as a small part of the normal or transient flora of the throat and alimentary tract.[5] A detailed characterization of this genus was given by Wickerman,[6-7] but the mechanism by which these organisms cause infections has not yet been determined.

There is a report of the isolation of *Hansenula anomala* from an infant with interstitial pneumonia.[3] We have presented another case in which *Hansenula anomala* was identified in the blood. This identification was confirmed by the Bureau of Laboratories of the New York City Department of Health and by the Culture Collection Research-Fermentation Laboratory (Peoria, Ill) of the US Department of Agriculture. Repeated isolation of *H anomala* in pure cultures of the pa-

tient's blood is highly supportive of our finding. The source of the infection could not be determined. A yeast, together with *P aeruginosa*, was found in sputum culture, but it was not identified at the time. To our knowledge, this is the first published report of *Hansenula anomala* fungemia.

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Reversible, nonoliguric acute renal failure in a patient with rheumatoid arthritis and renal amyloidosis

TO THE EDITOR: The nonsteroidal anti-inflammatory drug naproxen has recently been implicated in impaired renal function. We describe a patient who received naproxen for rheumatoid arthritis, and in whom nonoliguric acute renal failure developed, which disappeared after cessation of drug therapy.

Case Report: A 72-year-old woman, who had rheumatoid arthritis of four years' duration, was admitted to the hospital for progressive weakness, dysphagia, and epistaxis of four weeks' duration. She had been taking naproxen, 500 mg daily, during the previous two months. Previously, she had received aspirin, indomethacin, and corticosteroids. There was no other relevant information in her medical history. Urinalysis and serum creatinine levels were within normal limits one year before admission. However, three weeks before this hospital stay, her serum creatinine level was 3.1 mg/dL.

A physical examination showed normal skin turgor, and swelling of the elbows, knees, and small joints of the hand with ulnar deviation. The patient's blood pressure was 140/90 mm Hg. Urinary output was 1,200 mL/24 hr; urinalysis disclosed a specific gravity of 1,006, a protein level of 3.5 g/day, and a few small hyaline casts; the urine culture was sterile. The hematocrit was 38%; white blood cell count, 9,500/mm^3 with 9% eosinophils; and platelet count, 840,000/mm^3. The results of other blood tests were as follows: blood urea nitrogen, 106 mg/dL; serum creatinine, 6.5 mg/dL; creatinine clearance, 8 mL/min; serum phosphate, 9.0 mg/dL, and serum uric acid, 9.5 mg/dL. The erythrocyte sedimentation rate was 135 mm/hr. A latex agglutination test for rheumatoid factor was positive in a titer of 1:5,000. Serum complement activity was normal. An isotopic renogram showed bilateral, normal-sized kidneys with poor excretion and no evidence of urinary obstruction. Electrocardiography, a chest radiograph, an upper gastrointestinal radiographic series, and a muscle biopsy disclosed no abnormalities.

Naproxen therapy was stopped, and the patient was given aluminium hydroxide therapy. There was a gradual decline in the blood urea nitrogen level during the subsequent four weeks, to 20 mg/dL, and a simultaneous fall in the serum creatinine level to 1.4 mg/dL; phosphate levels fell to 3.5 mg/dL; and uric acid levels fell to 5.3 mg/dL. However, protein excretion increased to 6.7-8.8 g/day, and the total serum protein level fell to 5.0 g/dL, with 2.9 g/dL of serum albumin.

A renal biopsy was performed one month after admission. On light microscopy, amyloidosis was demonstrated in most of the glomeruli, with thickened middle-sized arteries and normal interstitial matrix (Fig 1). Electron microscopy confirmed the presence of amyloid filaments (Fig 2). Immunofluorescent staining disclosed immunoglobulin G (IgG) and complement (C3) in parts of the glomeruli and in the basal membrane of tubules and arteries. Renal function was stable during the next two months.

Discussion. This patient had a complex form of renal disease. Although renal failure is a frequent complication of collagen disease, such as systemic lupus erythematosus and polyarteritis nodosa, it is uncommon in rheumatoid arthritis. The main causes of renal failure in rheumatoid arthritis are amyloidosis and drugs.

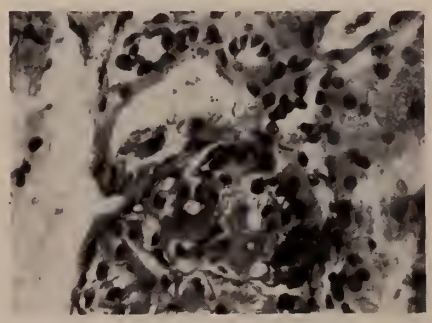

FIGURE 1. Amyloid deposition in the mesangium of glomerulus (Congo red stain, original magnification X 160).

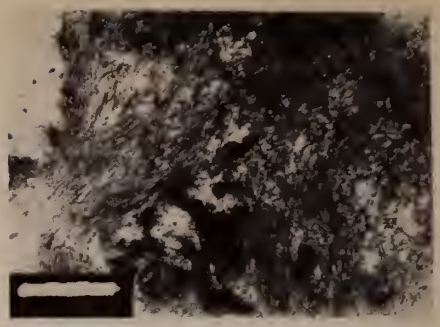

FIGURE 2. Electron micrograph of renal biopsy showing amyloid fibrils (original magnification X 12,500).

In the patient described, renal amyloidosis was manifested clinically by massive proteinuria. In addition, nonoliguric acute renal failure developed while the patient was receiving naproxen therapy.

Renal amyloidosis is diagnosed in approximately 5-10% of patients suffering from rheumatoid arthritis,[1] and in 70% of patients with rheumatoid arthritis and proteinuria.[2] Uremia is a uncommon symptom of amyloidosis and is usually fatal.

The adverse effects of nonsteroidal anti-inflammatory drugs on the kidney include acute renal failure, nephrotic syndrome, interstitial nephritis, and chronic renal injury with papillary necrosis.[3] Naproxen has recently been implicated in transient renal dysfunction,[4] acute interstitial nephritis,[5-7] and papillary necrosis.[8]

In two previously reported cases of reversible acute renal failure following naproxen administration,[8,9] interstitial nephritis was found on biopsy, and the patients were receiving other medications at that time. This patient differed in that she was receiving no other drug at the time and histologic analysis of the renal biopsy revealed amyloidosis. For all three patients, recovery time after cessation of naproxen therapy was short: one month.

In the patient reported here, we suggest that amyloid deposition rendered renal function more susceptible to prostaglandin activity. Subsequent prostaglandin suppression by naproxen diminished glomerular filtration and caused nonoliguric acute renal failure, which was promptly resolved on cessation of the drug.

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Dermatofibrosarcoma protuberans: An unusual presentation

TO THE EDITOR: Dermatofibrosarcoma protuberans accounts for 1% of all skin tumors.[1] It is a locally aggressive tumor of the dermis with definite metastatic potential. Bezecny[2] is credited with reporting the first case of metastasis. We report a case of dermatofibrosarcoma protuberans with metastasis to the liver and lung.

Case Report. A 76-year-old woman had become increasingly short of breath for the past three months and also had a painful mass on her back. On examination, she was dyspneic, anicteric, and had nodular hepatomegaly. The mass was 3 × 3 cm and located below the inferior angle of the right scapula. It was fixed to the skin and subcutaneous tissue, was not ulcerated, and did not have any satellite nodules.

A complete blood count, SMA-6, and coagulation profile were within normal limits. Liver enzyme levels were normal except for a raised alkaline phosphatase level (292 U/L). The level of carcinoembryonic antigen was within normal limits. A chest radiograph showed multiple nodules; these were

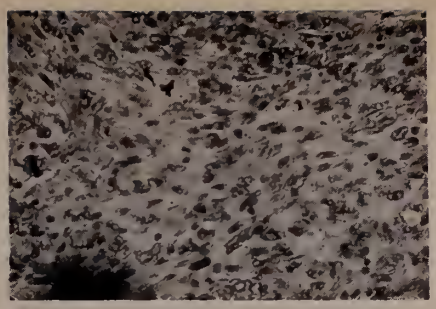

FIGURE 1. Skin biopsy showing spindle cell tumor (hematoxylin-eosin stain, original magnification × 10).

confirmed by a computed tomographic scan of the chest. Multiple filling defects were also seen on a Tc^{99} scan of the liver.

An excision biopsy of the mass showed tumor invasion into the lower dermis and upper subcutaneous fat with vessel involvement. Spindle cells in a storiform pattern characteristic of dermatofibrosarcoma protuberans were seen (Fig 1). Five mitoses per high power field were observed. A liver biopsy, done with a Menghini needle, showed neoplastic features identical to that of the skin tumor (Fig 2).

Discussion. Darrier and Ferrand[3] first identified this tumor as a definite clinicopathologic entity in 1924. In 1925, Hoffman[4] coined the term dermatofibrosarcoma protuberans. The tumor is seen most often in the fifth decade of life as a firm multinodular mass with purplish discoloration of the overlying skin. It is commonly located on the trunk and proximal extremities. The tumor is usually fixed to the skin and subcutaneous tissue. It may also be present as an ulcer or as a central nodule with satellite lesions.

The histogenesis of dermatofibrosarcoma protuberans is believed to be histiocytic, with fibroblastic arrangements resembling the weaving of a straw hat, hence the term storiform.[5] Others believe it to be of neurogenic origin, on the basis of cytoplasmic melanin within neural tissue. Another theory describes the tumor as a storiform neurofibroma.[6]

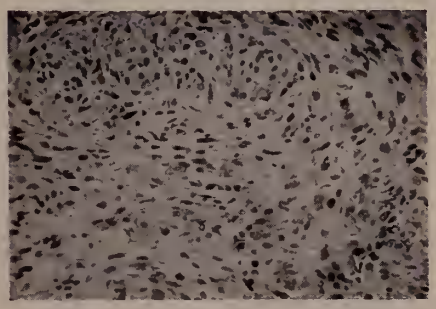

FIGURE 2. Liver biopsy showing storiform pattern and mitotic figures (hematoxylin-eosin stain, original magnification × 10).

The pathognomonic feature is the cartwheel arrangement of cells described in all 115 cases by Taylor[7] in 1952. Anaplasia is rare, and there are zero to four mitoses per high power field.

The natural history of this tumor is that of a low grade sarcoma with a marked tendency to recur (10–49%).[7] The period of recurrence is commonly one to three years after excision. Of 402 cases studied by Brenner et al,[8] 23 had visceral metastases.

Current therapy consists of wide local excision.[9] Skin grafting may be required in some cases. Doxorubicin and decarbazine have been administered to patients with this disorder. After excision of the tumor, patients should be closely followed for possible recurrence.

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Acknowledgments. The authors thank Dr Arthur Allen, Chief of Pathology at Interfaith Medical Center, for reviewing the histologic slides, and Mr Faizi Siddiqi for typing the manuscript.

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Micropsia

TO THE EDITOR: The letter, "Micropsia: Lilliput revisited," by J. M. Schneck, MD (1986; 86:321), described the psychogenic micropsia referred to by novelists. Lest the reader be misled into believing that all patients with dis-

tortion of visual perception (metamorphopsia) have a psychogenic etiology thereof, I would refer them to my article,[1] as well as to Golden's subsequent review.[2] Two of my three original cases of infectious mononucleosis presenting as "Alice in Wonderland" syndrome had first been referred by other doctors, without thorough examination, to psychiatrists because of this bizarre presentation. Objects, indeed, did seem to shrink or expand, to advance or retreat, as they did for Lewis Carroll's protagonist, young Alice. My physical examination revealed, and laboratory tests confirmed, the diagnosis in each case.

This symptom complex, incidentally, has been recognized so often since then that, on Long Island, the combination of metamorphopsia and infectious mononucleosis has sometimes been called "Copperman's Syndrome."

I would urge readers to rule out physical illness, migraine, epilepsy, and, of course, hallucinogen ingestion, before psychiatric referral for metamorphopsia.

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In reply. Regarding comments by Stuart M. Copperman, MD, in response to my letter to the editor of the *Journal*, please note that I am aware that micropsia need not be "psychogenic." Among my published articles on micropsia, one mentions illnesses with which micropsia may be associated.[1] Listing various illnesses which at times incorporate micropsia was not relevant to the main point of my communication on Lilliput revisited, and thus such illnesses were not mentioned.[2] The emphasis in my letter to the editor was on "psychogenic" micropsia. The fictional characters involved in my report obviously were not experiencing the phenomenon in an "organic" context. I agree that patients describing microptic episodes to physicians should have appropriate physical examinations. Physicians should also be aware of "psychogenic" micropsia as a possible diagnosis.

The patients I have seen had consulted physicians who could offer no answer to their questions and were not familiar with micropsia. I suspect that the percentage of patients with micropsia in association with infectious mononucleosis would be quite small in proportion to the total number of patients with micropsia. Most patients with this symptom have a "psychogenic" disorder. For these patients, an understanding of the psychopathology should be significant.

Some of the illnesses with which micropsia may be associated were observed decades ago. For example, Wechsler, in his textbook of neurology, wrote that micropsia or macropsia may occur with tumors of the temporal or temporosphenoidal lobe. He said also that "Micropsia or Lilliputian visions have been described as petit mal attacks, though they more commonly occur as aura."[3]

One might conjecture that regardless of the types of illness with which micropsia is associated, the symptom may be a reflection of conscious or unconscious anxiety in relation to awareness of illness. At the same time it would serve neuropsychologically as a coping mechanism by patients in an attempt to master such anxiety by symbolically distancing themselves from a problem setting, no matter how ineffective the effort may be.

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SOCIAL CONTROLS AND THE MEDICAL PROFESSION

Edited by Judith P. Swazey and Stephen R. Scher. 268 pp. Boston, Oelgeschlager, Gunn & Hain, Inc, 1985. $27.50 (hardcover)

In recent decades, the rise of consumerism, anti-establishment sentiments, and the dethroning of "the experts," have made inroads on previously insulated, elitist professions. Their autonomy and self regulation have come under critical scrutiny by a better-educated public. This is reflected for medicine, in part, in such societal responses as the sick doctor statutes enacted by 37 state legislatures and, reactively within the profession, in the American Medical Association sponsored programs for the rehabilitation of impaired physicians.

It is the latter phenomenon and its philosophical underpinnings that in the moral professions, only fellow professionals may evaluate the deviant behavior of one of their number. Therefore such deviance is considered nonvolitional and sick, rather than evil, and requiring treatment, rather than deserving punishment. This is analyzed by psychiatrists, surgeons, philosophers, sociologists, lawyers, and historians in this book.

The papers in this volume are products of a series of 11 interrelated conferences held over a two-year period with the sponsorship of the Project on Social Controls and the medical profession under the aegis of Medicine in the Public Interest. The editors (and project officials) are, respectively, a PhD in the History of Science (Swazey) and a PhD in Philosophy (Scher).

The book is divided into two parts: Part I, entitled "Comparative Perspectives on Professions and Their Governance," and Part II, entitled "Competence and Impairment in the Medical Profession." The individual contributions are well written, substantive, and of consistently high quality. However, the collection as a whole does not escape the traps inherent in collating disparate units, independently prepared for a wide range exploratory effort by representatives of diverse fields under a single rubric. In a simultaneous effort to provide breadth of outlook and depth of inquiry, the book suffers in Part I from a diffuseness of focus (interesting but basically extraneous material about the professions of law, research science, and the ministry), and in Part II from considerable duplication and overlap as well as a narrower construction of social controls than the reader might have anticipated from the title.

Social Controls and the Medical Profession, as a title, implicitly bears the promise of a comprehensive investigation of the internal methods of self governance employed by medicine, the external controls (formal and informal) exercised by society on medicine, and possibly also, in the words of the sociologist I. K. Zola, "the medicalization of society and with it, the growth of medicine as an institution and instrument of social control." In reality, by editorial choice, this book confines itself largely to the first of these concerns and even more specifically to a particular internal social control mechanism: the medicalization of physician deviant behavior.

Within these parameters, however, the presentations are excellent and raise a number of pertinent questions for further exploration (a declared intent of Dr Swazey's):

- Does some deviant behavior perhaps stem from voluntary risk-taking behavior on the part of MDs and therefore not qualify for the protective cover universally offered the impaired physician?
- Is this medicalization of physician problem behavior only a cynical device to maintain control within the profession rather than allow external social agencies to discipline MDs?
- Ought patient complaints be given greater credence in determining physician fitness to practice or are MDs properly dismissive of them as difficult or ignorant?
- Does deviance or impairment consist only of proven technical incompetence or are issues of style and manners relevant?
- What are the boundaries of acceptable error or mistake rates for physicians?
- Are impaired physician programs, which deal only with individual problems in idiosyncratic fashion, overlooking structural problems in the organization of medical training and practice that may help to precipitate such behavior?

As Renee Fox, professor of Social Sciences at the University of Pennsylvania, says in the concluding article, "We have only begun to understand the multiple facets of physicianly competence, its dynamics and ecology, how it is taught and learned, its powers and limitations, its potentialities for benefit and for harm and how it can be used by physicians continually to heal themselves along with their patients."

Future studies must pursue the issues delineated by this one.

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INFERTILITY. A PRACTICAL GUIDE FOR THE PHYSICIAN

Second Edition. Edited by Mary G. Hammond, MD, and Luther M. Talbert, MD. 208 pp, illustrated. Oradell, NJ, Medical Economics Co, 1985. $17.50 (paperback)

This small, soft-cover book is a succinct and practical guide for students, residents, and practicing physicians who care for patients with infertility. In almost all respects the book fulfills its overall purpose. Both editors—Drs Hammond and Talbert—are well known and respected throughout the country in the areas of infertility and reproductive endocrinology. They have with them in the development of this book a number of authors who have contributed chapters and who are as expert in their specific areas as are the editors. It is interesting to note that there are numbers of textbooks on infertility but there are very few guide books that so concisely and practically handle the entire issue of infertility. This book is not designed to be an exhaustive treatise; rather it is meant to be a guide in the treatment of infertility. Clearly this is a major advantage of the work.

The contents of the book consist of general topics of infertility such as "The Arithmetic of Infertility Therapy" and "Doctor-Patient Relationships in Infertility." It also covers evaluation

of both male and female factors in infertility, devoting a fair amount of space to the question of sperm testing and artificial insemination. Most of the book, however, deals with the female and the question of peritoneal (pelvic, uterine, cervical, tubal) factors and their diagnosis and treatment. It very nicely handles, for example, the question of tubal factors in infertility. The chapter is well illustrated, with heavy stress placed on the recording of the findings at the time of assessment of the pelvis. This is an area that is frequently neglected. Clearly the purpose of this book is not to instruct one in the intricacies, complexities, and subtleties of tubal surgery. However, a perusal of the chapter on tubal factors will enable one to gain a very general but highly informative overview of the entire issue.

Although one chapter is devoted to ovulatory dysfunction, it is a quite nice chapter with clear and appropriate discussions of a variety of anovulatory entities and their appropriate therapies. There are two chapters on endometriosis and in vitro fertilization, both of which are good assessments of the current status of these entities.

I would highly recommend this book to individuals interested in the general problem of infertility who need a clear and broad overview. It is well done, complete, and thoughtful.

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THE FAMILY, THE PATIENT, AND THE PSYCHIATRIC HOSPITAL: TOWARD A NEW MODEL

Formulated by the Committee on the Family, Group for the Advancement of Psychiatry. 106 pp. New York, Brunner/Mazel Publishers, 1985. $11.95 (softcover)

This short paperback is a reminder to the professional and an explanation to the families of hospitalized patients with psychiatric illnesses of the importance of a family-oriented approach (ie, one that includes family members other than the designated patient in implementation of the treatment plan). In the words of the book, "the evidence in favor of a family-oriented approach is now so substantial as to mandate its addition to the traditional treatments" and, "without an alliance between the hospital caregivers and the family, the gains of a short hospitalization are all too likely to be lost."

Written as it is by the Committee on the Family of the GAP, the authors have no need to further demonstrate their qualifications for writing such a book.

As an addition to the medical literature on the subject, the extensive bibliography suggests that, as mentioned, its value is chiefly as a reminder of all of the work that has been published supporting the authors' thesis. However, most interesting and innovative is the appendix, a 17-page guide for consumers that should be of enormous help in eliciting a cooperative response from families. As we have all experienced, the family can not only *not* help in the patient's treatment, but may actively obstruct it by refusing to be involved, by preventing or interrupting hospitalization, or by undermining treatment. The guide is most useful in showing the reader how to approach the family in a nonthreatening way so that they will not feel accused as the cause of the patient's illness, but rather that they have difficulties in dealing with a family member who is disruptive, antisocial, or otherwise troublesome.

As stated, this short report first follows the family "through the process of evaluation and decision-making for or against hospitalization versus another alternative—partial hospitalization." The characteristics of a family-oriented treatment program are described, followed by a presentation of the essential aftercare programs. Finally, the report discusses the ethical dilemmas surrounding the choice between a family or individual approach. It also discusses the ethical dilemmas involved in communication among members of the staff, the question of confidentiality, and how it might be breached.

These issues, with their inherent internal conflicts, are clearly discussed, although it is recognized that there are no easy answers as, for example, in cases where what is good for the family is bad for the patient.

The argument of the book is that since both administrative and fiscal forces are presently leading to shorter hospitalizations and increasingly early discharges of patients, the therapist is put in a bind about where his responsibility lies. The authors believe that "family-oriented treatment must include an ethical commitment to all members of the family" even when individual interests clash. How this is to be accomplished is not clearly stated, and the inclusion of case reports points out in a concrete way the thorny aspects of this issue.

The report is not unique. The bibliography refers to more than 40 papers and sections in standard tests. But it goes perhaps further in being more extensive in its treatment of the subject and pointing to more ethical dilemmas. Here is food for thought and material for further papers. Can we offer our patients the guarantee of confidence and if not, what happens? More directly, at what point lies a clash between individual rights and the mental health worker's decision about what is best for the patient? Indeed, what are the moral and political consequences of our knowing what is best, and attempting to enforce it? Thought-provoking? An understatement.

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THE BEAST IN A CAGE OF WORDS

Edited by Alan Cohen, MD, with an introduction by Donald Junkins. 36 pp. Belchertown, Mass, Sun's Nest Press, 1985. $5.00 (softcover)

Nuclear holocaust, the "final epidemic," concerns every citizen of the earth, and certainly every physician. Yet we shrink from contemplating it, because its horror may overwhelm, depress, and even paralyze us. As busy physicians, we cannot afford that, either emotionally or practically. Unfortunately, we can less afford to ignore the problem. The impact of publications on this topic in the *Journal of the American Medical Association*, and the recent awarding of the Nobel Peace Prize to International Physicians for the Prevention of Nuclear War, forcefully recall how effectively the voices of physician-citizens command attention, when speaking with authority.

Dr Alan Cohen, an internist from Chicopee, Massachusetts, has done his fellow physicians two services by editing a short volume of poems on nuclear war. Although physicians wrote less than one half of the poems, the book was appropriately published with the support of Physicians for Social Responsibility. This group is the American affiliate of International Physicians

for the Prevention of Nuclear War. Dr Cohen serves as an officer of his local chapter.

All of the poems in the book show accomplishment and craftsmanship. Most frighten the reader, but none are numbing. Many offer hope and encouragement, if only we will act. One does not despair on reading these poems, nor turn away, grasping for sunlight and relief. Nor do they lull the reader. Nuclear war joins uncomfortable topics: genocide, torture, murder, and injustice.

Sharon Thomson's poem, "The End," conjures the reality of megaton explosions more vividly than the television drama, *The Day After*, ever could. Berniece Bixler's "After The Bombs: Last Freefall" creates a watercolor sense, half-fantasy, that lingers in one's memory. "To Monitor The Effects" by Bill Christopherson will strike a responsive nerve in physicians, and will outrage those who infer a generalization from it. Joan Dobbie's "This Night" provides perhaps the most lyrical, immediate, and personally poignant reflection of all. Several poems recall past, actual nuclear bombings of the two Japanese cities and of our not quite uninhabited test sites. Inevitably, some efforts fail. Herbert Clark's "Terminal Intelligence" strikes only one note and without poetry. The strong stuff of this book need not be a deterrent; the reader will be gratified to have experienced it.

This brings me to Alan Cohen's second service to us all. He has made a contribution to the growing practice of the arts by physicians. His own poem, "The Garden of Eden," is more predictable than "Autopsy" (*N Engl J Med* 1977; 17:400); but then, this poem has the extra task of bespeaking social and political consciousness. The absence of preaching here and throughout the volume constitutes an amazing achievement, given the intensity of the authors' feelings about the issue.

Even physicians who never read poetry, who have had no contact with antinuclear activity, and who feel "hawkish," will enjoy the richness, the new viewpoints, and the accessibility of the writing. The pretentious, "artsy," and recondite "Foreward" [sic], and several typographical errors could have been avoided through better editing. Most readers will take pride in our colleague, whose efforts brought this important collection to light. Those who share his outlook will gain further gratification from the knowledge that revenues from sales of the book support the antinuclear movement. But in the end, we sample the arts for pleasure, not duty, and these deeply felt, beautiful poems provide pleasure while keeping us aware of a great issue, perhaps *the* greatest issue of our times.

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TECHNIQUES IN ORTHOPEDICS: ARTHROSCOPIC SURGERY UPDATE

Volume 5. Edited by John B. McGinty, MD. 153 pp, illustrated. Rockville, Md, Aspen Systems Corp, 1985. $36.50 (hardcover)

This book contains 17 chapters that include the latest information on instrumentation for the shoulder, arthroscopy of the elbow and ankle, and techniques for the management of tibial plateau fractures. In addition, there are well-written chapters on basic arthroscopic techniques of the knee.

In going over these chapters, some subjects appear to require further clarification. It is not clear how removal of shredded articular cartilage relieves pain in release procedures and chondromalacia since there are no pain-bearing fibers in articular hyaline cartilage, as reported by Dr Lanny Johnson in 1977. Grade 3 chondromalacia with arthroscopic patellar debridement is thought to relieve anterior knee pain, but it appears that it is not known how this occurs.

With regard to malalignment procedure releases, the text indicates that functional rehabilitation is more important than any particular type of arthroscopic procedure. One criticism I have in this regard relates to page 53, where a quadriceps stretch with the heel touching the buttock is recommended. This actually produces significant wear contact against the patella and the posterior tibia and femur. It would have been better to advocate hip extension so that the quadriceps could be maximally stretched.

The chapter by Guhl on how to manage articular lesions arthroscopically is excellent. The technical advances described are particularly helpful and may be used by all qualified arthroscopists who see adolescents with knee problems and treat large osteochondral fractures.

The chapter on the blood supply of the meniscus is written by Arnoczky. It is repetitious of information presented in several text papers published in 1982, 1983, and 1985. Chapter 8 on arthroscopic meniscus repair by Henning and his group has excellent diagrams and discusses common errors. I noted with interest that 95% of the 168 menisci described could be repaired. Long term follow-up of these cases should be made since the effectiveness of the procedure has not yet been proven.

In the tenth chapter Caspari discusses arthroscopic management of some tibial plateau fractures, and this certainly may be a useful tool. However, it must be pointed out that there are only a limited number of fractures that may be treated in this manner. Many excellent fracture surgeons are not arthroscopists and should not try to follow these suggestions. The arthroscopic management of anterior cruciate ligament tears is described by Tippett. It is emphasized that ligaments may be repaired in this manner; however, only 18 cases are described. It is too soon to make any judgments on this. Moreover, I think that the paramount role of the capsular contributions for instability should not be forgotten when one gets into the arthroscopic use of exogenous materials for the deficient anterior cruciate. Arthroscopy of the ankle and elbow is also described.

Notwithstanding these comments, this update should be in the hands of anyone who is doing arthroscopic surgery. The need for additional research in the development of arthroscopic surgery is emphasized in the final chapter. It is a philosophical chapter, pointing out many current limitations that still exist regarding the use of arthroscopy.

This work has excellent illustrations, is well written, and is of value to those physicians employing arthroscopy. Unfortunately, the information presented is incomplete and assumes considerable experience on the part of the clinician performing the arthroscopy. The general orthopedic surgeon and those interested in trauma will not find much of value in this book that cannot be found in standard texts on arthroscopy. Updates, however, are useful for their descriptions.

Woefully lacking in this book is a discussion of competency, diagnostic accuracy, quality assurance, and adequate arthroscopic diagnosis. This is a serious problem that is found in many other arthroscopic surgical books. Cost control is also needed as part of the ap-

proach to prevent overuse of the arthroscopic procedure. I believe the author implies this in the last paragraph of his preface.

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CHANGE OF HEART. THE BYPASS EXPERIENCE

By Nancy Yanes Hoffman. 480 pp. New York, Harcourt Brace Jovanovich, 1985. $17.95 (clothcover)

Toward the end of this book the author notes that "Bypass is controversial, both medically and economically." With that caveat out of the way, the main business of the book can be examined. Almost 400 pages of this volume describe how 21 "travelers," people who have had single or multiple bypass operations, dealt with the situation. Each individual responds to questions posed by the author in personal interviews. These people detail their lifestyles, their stresses, their genetic background, their preparation or lack of preparation, and the help or hindrances along the way to surgery and recovery. While most of the patients were men, there were a few women, including a housewife and a nun. The men had diverse occupations—physicians, an army officer, businessmen, an educator, and people in communications. The ages of the individuals studied ranged from 30 to 70 years with most of the patients in their 40s and 50s. One person had had three bypass operations and two persons had had two.

These travelers, so-called with an allusion to the travelers in Chaucer's *Canterbury Tales*, recount their innermost feelings to the author and seek to provide guideposts, counsel, and comfort to others afflicted with coronary problems that could lead to making a decision about bypass surgery. To this reader, that is the heart and soul of this book. Any person concerned with the interactions between healers in the health care system and patients and their families can derive a wealth of insight into the concerns of human beings during a medical crisis. Actually, the effects of the bypass surgery are secured from four to 15 years after the event. Unfolding before us is a litany of questions going unanswered and topics such as sex after surgery never being raised at all. Of course, that is balanced by examples of solid interactions between patients and their caregivers.

Even though it is difficult to compete with the glamour of surgery, the author does stress the prevention of coronary heart disease through the elimination of risk factors such as smoking, controlling high blood pressure, reducing stress, and following a diet designed to reduce the intake of fats. A diet guide is included as well as a listing of type A characteristics so that readers can modify their eating habits and life situations.

In addition, this book discusses what type of hospital to choose for bypass surgery, noting along the way that many hospitals could be suboptimal. More than 20 questions are listed for patients to ask of their internist, cardiologist, surgeon, and anesthesiologist, with each question labeled for the appropriate physician. Relief of common complaints after bypass is also addressed with attention to coughing, breathing, scar irritation, and communicating with people. Nine quick maneuvers are identified to promote concentration and relaxation. Noting physician reluctance to discuss sex, the author lists eight suggestions for sexual relations along with warning signals to watch for in case of overexertion. There is also an activity sheet that may be given to the physician to go over the recommended items with the patient. There is even a glossary of medical terms for those who are not familiar with the argot of bypass surgery.

Early on the author states that the book is not an argument for or against bypass. However, the feeling emerges that it is certainly a procedure that has helped many people to live longer and fuller lives. Nevertheless, avoiding (as it does) the pitfalls of debating the value or nonvalue of bypass surgery, this book is recommended for the touching human stories of people and their interactions with the medical care system in the United States. Reading the bulk of the tales of the travelers should provide telling insights for all professionals concerned with caring for the ill and their families.

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Data on medical liability reported

The American College of Physicians (ACP) has released the findings of a study to determine the basis of the increasing number of malpractice claims. According to the study, most lawsuits among internists result from the failure to accurately diagnose diseases such as cancer—primarily cancer of the breast, lung, or colon. Another common reason for malpractice claims is harm caused the patient due to inappropriate drug therapy. For gastroenterologists, lawsuits are most often associated with complications that arise during endoscopy or biopsy. "Improperly performed procedures" account for the most lawsuits plaguing cardiologists, according to the report.

The ACP has drawn several disturbing conclusions from the data: All medical specialties are facing an increasing number of malpractice actions, with larger awards being sought; medical liability premiums are continuing to rise; and, of all paid malpractice claims, 78% resulted from injuries sustained in hospitals.

AMA proposed ban on tobacco advertising gains support

A recent ruling by the US Supreme Court supports the constitutionality of a ban on cigarette advertising. The ban, proposed by the American Medical Association, has faced stiff opposition from the tobacco industry and has been alleged to violate the First Amendment of the Constitution. However, the Court ruled that a ban on gambling advertisements imposed in Puerto Rico does not violate the right of free speech.

In its ruling, the Court implied that states have the right to ban advertising of other "harmful" products, which might include tobacco. This legal precedent should serve as useful ammunition in the fight against cigarette advertising.

Federal legislation to ban tobacco advertising was introduced in Congress this summer. In a letter to the *Journal of the American Medical Association*, Vincent Blasi and Henry Paul Monaghan of Columbia University School of Law, both specialists in constitutional law, defend the constitutionality of a federal ban on promotional cigarette advertising.

The authors stress the distinction between freedom of speech and freedom of commercial speech. They suggest that tobacco advertising is misleading in its treatment of the health effects of smoking, and that a ban on such promotional activity would be in the best interest of the public health. Citing the powers of Congress and previous Supreme Court rulings, Blasi and Monaghan conclude that a ban on cigarette advertising does not conflict with the tobacco industry's first amendment rights.

Hepatitis B vaccines

People at risk of acquiring hepatitis B can now choose from two safe forms of protection. Heptavax-B, a vaccine made from the plasma of patients with hepatitis B, has been found to carry no risk of infection with AIDS. Recombivax HB, a new genetically engineered vaccine, has now been approved for commercial use by the Food and Drug Administration.

Heptavax-B, introduced in 1982, was the first hepatitis B vaccine to come to market and has been shown to be very effective. To date, about one million people in the US have received the vaccine. Questions as to the safety of Heptavax-B arose because people in the high risk groups for acquiring AIDS were among the donors of the blood used to prepare the vaccine. Investigators at the Centers for Disease Control in Atlanta have concluded that Heptavax-B does not carry the AIDS virus, and therefore transmission of the disease is not a threat. This conclusion is based in part on the following findings: the vaccine contains no genetic material related to the AIDS virus; the inactivation procedures used to produce the vaccine would render the AIDS virus harmless; and people inoculated with the Heptavax-B vaccine have not developed antibodies to the AIDS virus.

Fears of transmitting blood-borne infectious agents are unfounded with Recombivax HB. The vaccine is composed of a protein component of the hepatitis B virus. Rather than being isolated from infectious plasma, the protein is manufactured by yeast cells that, as a result of genetic engineering, contain a gene from the hepatitis B virus. Recombivax HB is the first genetically engineered vaccine to be licensed for use in humans.

NEWS BRIEFS are compiled and written by Vicki Glaser.

OBITUARIES

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Lester Irwing Abend, MD, Kew Gardens. Died June 11, 1986; age 63. Dr Abend was a 1947 graduate of State University of New York Downstate Medical Center, New York. He was a Fellow of the American Psychiatric Association and a Diplomate of the American Board of Psychiatry and Neurology. His memberships included the American Society of Adolescent Psychiatry, the American Academy of Child Psychiatry, the Association for Advancement of Psychotherapy, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Hans Fritz Bauer, MD, Syracuse. Died April 10, 1986; age 89. Dr Bauer was a 1923 graduate of Hamburgische Universität Medizinische Fakultät, Hamburg. He was a member of the American Academy of Family Practice, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Albert Theodore Berg, MD, Staten Island. Died May 19, 1986; age 81. He was a 1932 graduate of the University of Michigan Medical School, Ann Arbor. Dr Berg was a member of the Society of Nuclear Medicine, the Richmond County Medical Society, and the Medical Society of the State of New York.

Herbert Irwin J. Berner, MD, Brooklyn. Died February 21, 1986; age 82. Dr Berner was a 1929 graduate of New York University College of Medicine, New York. He was a Fellow of the American College of Physicians and a Diplomate of the American Board of Pediatrics and the American Board of Physical Medicine and Rehabilitation. His memberships included the American Academy of Pediatrics, the American Academy of Physical Medicine and Rehabilitation, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Louis F. Bishop, MD, New York. Died June 1, 1986; age 85. He was a 1925 graduate of Columbia University College of Physicians and Surgeons, New York. Dr Bishop was a Fellow of the American College of Cardiology, the American College of Physicians, the American College of Chest Physicians, and the American College of Angiology, and a Diplomate of the American Board of Internal Medicine. His memberships included the New York Academy of Medicine, the New York Cardiological Society, the New York Gastroenterological Society, the Pan American Medical Association, the American Academy of Compensation Medicine, Inc, the Academy of Psychosomatic Medicine, the New York County Medical Society, and the Medical Society of the State of New York.

Philip Vincent Buckley, MD, Poughkeepsie. Died June 6, 1986; age 77. Dr Buckley was a 1933 graduate of Georgetown University School of Medicine, Washington, DC. He was a Diplomate of the American Board of Radiology and a member of the Dutchess County Medical Society and the Medical Society of the State of New York.

James Caroscio, MD, New York. Died June 1, 1986; age 40. He was a 1973 graduate of State University of New York Upstate Medical Center, Syracuse. Dr Caroscio was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Academy of Neurology, the New York County Medical Society, and the Medical Society of the State of New York.

John Andrew Davis, MD, New York. Died November 10, 1985; age 89. Dr Davis was a 1925 graduate of Howard University College of Medicine, Washington, DC. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Robert Carl Eliot, MD, Brewster. Died February 17, 1986; age 77. Dr Eliot was a 1934 graduate of the University of Glasgow Medical Faculty. He was a member of the Putnam County Medical Society and the Medical Society of the State of New York.

Edward Paul Feder, MD, Sarasota, Florida. Died April 10, 1986; age 87. He was a 1926 graduate of State University of New York Downstate Medical Center, New York. Dr Feder was a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Edward Joseph Feely, MD, Bath. Died May 16, 1986; age 79. He was a 1934 graduate of Georgetown University School of Medicine, Washington, DC. Dr Feely was a Diplomate of the American Board of Radiology and a member of the Radiological Society of New York State, the Pan American Medical Association, the Radiological Society of North America, Inc, the Steuben County Medical Society, and the Medical Society of the State of New York.

Alfred Lewis George, MD, Batavia. Died June 5, 1986; age 76. Dr George was a 1934 graduate of the University of Buffalo School of Medicine. He was a member of the Medical Society of the County of Genesee and the Medical Society of the State of New York.

Seymour Goldenberg, MD, Eastchester. Died June 23, 1986; age 73. Dr Goldenberg was a 1939 graduate of Eclectic Medical College, Cincinnati. He was a Fellow of the American College of Anesthesiologists, a Diplomate of the American Board of Anesthesiology, and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the New York County Medical Society, and the Medical Society of the State of New York.

John Henry Heldt, MD, Sarasota, Florida. Died June 16, 1986; age 80. Dr Heldt was a 1930 graduate of Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia. He was a member of the Nassau County Medical Society and the Medical Society of the State of New York.

Paul Henkind, MD, New Rochelle. Died June 25, 1986; age 54. He was a 1959 graduate of New York University College of Medicine, New York. Dr Henkind was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Ophthalmology. His memberships included the New York Society for Clinical Ophthalmology, the New York Academy of Medicine, the American Academy of Ophthalmology and Otolaryngology, the Bronx County Medical Society, and the Medical Society of the State of New York.

Harold Wallis Jayne, MD, Sidney. Died May 23, 1986; age 64. Dr Jayne was a 1947 graduate of the University of Rochester School of Medicine and Dentistry. He was a Diplomate of the American Board of Internal Medicine and a member of the Delaware County Medical Society and the Medical Society of the State of New York.

George Amdee Jervis, MD, Stony Point. Died June 5, 1986; age 83. Dr Jervis was a 1927 graduate of Università Degli Studi di Milano, Facoltà di Medicina e Chirurgia. He was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Academy of Neurology, the American Psychiatric Association, the American Association of Neuro-Pathologists, the Society for Experimental Biology and Medicine, the Medical Society of the County of Rockland, and the Medical Society of the State of New York.

Edward J. Komora, MD, New York. Died June 19, 1986; age 80. He was a 1932 graduate of the New York University College of Medicine, New York. Dr Komora was a member of the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of the New York.

Fred Leventhal, MD, Westbury. Died June 4, 1986; age 58. Dr Leventhal was a 1953 graduate of the State University of New York Downstate Medical Center, New York. Dr Leventhal was a Diplomate of the American Board of Internal Medicine and a member of the New York State Society of Internal Medicine, the Nassau County Medical Society, and the Medical Society of the State of New York.

John F. Maloney, MD, New York. Died June 9, 1986; age 74. He was a 1941 graduate of Queens University Faculty of Medicine, Kingston. Dr. Maloney was a Fellow of the American College of Surgeons and a member of the New York Cardiological Society, the American Geriatrics Society, the New York County Medical Society, and the Medical Society of the State of New York.

George T. Obreshkow, MD, Port Jefferson Station. Died June 2, 1986; age 66. Dr Obreshkow was a 1944 graduate of Medizinische Fakultät der Universität, Wien. He was a member of the New York Cardiological Society, the American Occupational Medical Association, the New York County Medical Society, and the Medical Society of the State of New York.

Harry Plaskov, MD, Schoharie. Died May 14, 1986; age 86. Dr Plaskov was a 1939 graduate of Universität Basel Medizinische Fakultät. He was a member of the Medical Society of the County of Schoharie and the Medical Society of the State of New York.

Anton Joseph Pospisil, MD, East Northport. Died March 28, 1986; age 80. Dr Pospisil was a 1939 graduate of Universita Karlova Fakulta Lekarska, Praha. He was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Solomon Silver, MD, New York. Died June 10, 1986; age 83. He was a 1927 graduate of New York University College of Medicine, New York. Dr Silver was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine. His memberships included the New York Academy of Medicine, the American Thyroid Association, the Endocrine Society, the New York County Medical Society, and the Medical Society of the State of New York.

Arthur C. Smith, MD, Elmira. Died May 29, 1986: age 98. Dr Smith was a 1911 graduate of George Washington University School of Medicine, Washington, DC. He was a Fellow of the American College of Surgeons and a member of the Medical Society of the County of Chemung and the Medical Society of the State of New York.

Antanas Snieska, MD, Great Neck. Died June 11, 1986; age 68. Dr Snieska was a 1941 graduate of Vytauta Didziojo Universiteto Medicinos Fakelteto, Kaunas. Dr Snieska was a Fellow of the American College of Chest Physicians and a member of the American Thoracic Society, the New York County Medical Society, and the Medical Society of the State of New York.

S. Zelig Sorkin, MD, New York. Died May 30, 1986; age 79. Dr Sorkin was a 1934 graduate of Albert-Ludwig-Universität Medizinische Fakultät, Freiburg, Baden. Dr. Sorkin was a Fellow of the American College of Physicians, a Diplomate of the American Board of Internal Medicine, and a member of the New York Academy of Medicine, the Clinical Society, the New York Diabetes Association, the New York County Medical Society, and the Medical Society of the State of New York.

Ernest Abraham Stern, MD, Flushing. Died March 5, 1986; age 72. Dr Stern was a 1948 graduate of Universita Karlova Fakulta Lekarska, Praha. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Jacob H. Turner, MD, Bronx. Died May 12, 1986; age 86. He was a 1923 graduate of New York University College of Medicine, New York. Dr Turner was a Diplomate of the American Board of Pediatrics, and a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Steward A. Ver Nooy, MD, Cortland. Died January 1, 1986; age 88. Dr Ver Nooy was a 1925 graduate of Jefferson Medical College of Philadelphia. He was a member of the Radiological Society of New York State, the Cortland County Medical Society, and the Medical Society of the State of New York.

Milton Wallman, MD, Valley Stream. Died June 3, 1986; age 76. He was a 1936 graduate of Creighton University School of Medicine, Omaha. Dr Wallman was a Fellow of the American College of Allergists and a member of the American Geriatrics Society, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Andor A. Weiss, MD, Forest Hills. Died June 6, 1986; age 80. Dr Weiss was a 1935 graduate of Rush Medical College, Chicago. Dr Weiss was a Fellow of the American College of Physicians and a Diplomate of the American Board of Internal Medicine and the American Board of Physical Medicine and Rehabilitation. Dr Weiss was a member of the New York Academy of

Medicine, the New York Society for Physical Medicine and Rehabilitation, the American Academy of Physical Medicine and Rehabilitation, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Natacha J. Wilbur, MD, North Tonawanda. Died June 6, 1986; age 51. Dr Wilbur was a 1963 graduate of Faculte Francaise de Medecine de l'Universite de St Joseph, Beyrouth, Syria. Dr Wilbur was a member of the Medical Society of the County of Niagara and the Medical Society of the State of New York.

Victor Wolkin, MD, Rochester. Died April 24, 1986; age 76. He was a 1937 graduate of State University of Iowa College of Medicine, Iowa City. Dr Wolkin was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Orthopaedic Surgery. His memberships included the American Academy of Orthopaedic Surgeons, the Medical Society of the County of Monroe, and the Medical Society of the State of New York.

FROM THE LIBRARY

RADIOLOGY AND THE RADIOLOGIST OF THE FUTURE

The announcement of Professor Wilhelm Conrad Roentgen of his discovery of the x-rays, some two score years ago, opened the way for romantic adventure of human intelligence into unexplored fields. An account of the various steps of progress through which mechanical and chemical devices with creative understanding have advanced the use of the x-rays to the benefit of mankind would be both interesting and a source of inspiration. However, time and our present purpose do not permit of such review of this epoch, filled as it has been with the work of the pioneers, the pathfinders, and the martyrs with their individual and group contributions to what is now called Radiology. We dismiss this consideration of our subject with humble and generous acknowledgments to all of those men and women whose accomplishments have made possible so much precision and certainty in the practice of the healing art.

Reluctantly, we turn our discussion from the glories of the past to face the realities of the present. We serve a public whose mind is materialistic, practical. That public is interested in our Radiology for the service which it may render at the time of injury or sickness. And we, who engage in the practice of Radiology, may well consider our work from this social economic viewpoint. It is timely that we ask ourselves and our colleagues, these questions:

Is the present use of x-rays in medicine attaining the greatest possible good?

In what ways can the professional and social worth of this science be made more effective and helpful?

What, if any, are the influences which stand in the way of further desirable progress in such directions?

These must be intelligently answered if the Radiologist of the future is to be something more than a memory of an extinct branch of the medical profession. . . .

FREDERIC E. ELLIOTT, MD
(*NY State J Med* 1937; 37:1647–1651)

Attention Delegates
Your Next Meeting

The 181st Annual Meeting of the Medical Society of the State of New York will be held at the New York Hilton Hotel, New York City, on March 12–15, 1987

•

Nominating Committee, 1987

(The committee nominates Officers, Councilors, and Trustees of MSSNY, and Delegates to the American Medical Association.)

Member-at-Large—Daniel F. O'Keeffe, M.D., Warren, *Chairman*
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Third District—Thomas D. Pemrick, M.D., Rensselaer
Fourth District—Robert A. Reid, M.D., Warren
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Ninth District—Seymour R. Stall, M.D., Dutchess
Member-at-Large—David M. Benford, M.D., New York

Guidelines for authors

Originality

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media, and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089–1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

Preparation

An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

Categories

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

Figures

The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

References

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

References should be indicated in the text by superscript numbers following the name of the author (eg, Smith[2] reported two cases).

The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear in the text. When there are three or fewer authors, all should be listed; where there are four or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83: 925–927.
2. Behrman RE, Vaughn VC: *Nelson Textbook of Pediatrics*, ed 12. Philadelphia, WB Saunders Co, 1983, pp 337–338.

Review

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

Address correspondence to Pascal James Imperato, MD, Editor, *New York State Journal of Medicine*, P.O. Box 5404, 420 Lakeville Road, Lake Success, NY 11042.

Residents / Fellows

A $500 AWARD will be presented by the Medical Society of the State of New York to the intern, resident or fellow who submits the best paper on a clinical subject for the Society's 1986 Merit H. Cash Competition.

Entrants need not be members of the MSSNY but must be in training at a hospital within the State of New York.

Entries should be "sponsored" by a faculty member, and all papers submitted should be of sufficient quality to be considered for original publication in the *New York State Journal of Medicine.*

The deadline for receipt of entries is **December 1, 1986,** and the prize for the winning paper will be awarded at the MSSNY's annual meeting in March of 1987.

Address all entries to: Division of Scientific Activities
Medical Society of the State of New York
420 Lakeville Road
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Lake Success, NY 11042

Questions? Contact either the Division of Scientific Activities or MSSNY's Resident Physicians Section at (516) 488-6100.

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Resort, Maui. Info: Radiology Postgraduate Education, University of California, Room C-324, Third & Parnassus Ave, San Francisco, CA 94143-0628. Tel: (415) 476-5731.

ILLINOIS

Nov 8. **Workshop in Fiberoptic Endoscopy.** 7 Cat 1 Credits. *Nov 14–15.* **Hysteroscopy Workshop—Panoramic—Contact—Microcolpohysteroscopy: Didactic and Practical Hands-on Experience.** 10½ Cat 1 Credits. Info: Paula Puntenney, Alumni Center for Continuing Education, Northwestern University Medical School, 301 East Chicago Ave, Chicago, IL 60611.

Nov 16–19. **43rd Annual Meeting of the American Geriatrics Society and the 7th Annual Meeting of the American Federation for Aging Research.** Marriott Hotel, Chicago. Info: American Geriatrics Society, Room 1470, 10 Columbus Circle, New York, NY 10019. Tel: (212) 582-1333.

IOWA

Nov 10–14. **Intensive Course in Pediatric Nutrition.** Iowa City. Info: Samuel J. Fomon, MD, Department of Pediatrics, University of Iowa Hospitals, Iowa City, IA 52242. Tel: (319) 356-1831.

MASSACHUSETTS

Nov 10–13. **Broadening the Skills of the General Care Internist, V.** 21 Cat 1 Credits. Copley Plaza Hotel, Boston. Info: Course No. 606, American College of Physicians, PO Box 7777-R-0510, Philadelphia, PA 19175.

Nov 16–21. **Occupational Health Management.** Boston. Info: Office of Continuing Education, Department A, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115. Tel: (617) 732-1171.

MICHIGAN

Nov 16. **Sports Medicine and Youth: Sports Related Injuries; Sports Physical Exam and History.** Kellogg Center for Continuing Education, East Lansing. Info: Sandy Kilbourn, MSU College of Osteopathic Medicine, A306 E. Fee Hall, East Lansing, MI 48824. Tel: (517) 353-9714.

TEXAS

Nov 12–14. **Current Approaches for the Diagnosis and Treatment of Gastrointestinal Cancers.** Hotel Inter-Continental, Houston. Info: Office of Conference Services, Box 131, M.D. Anderson Hospital and Tumor Institute, 6723 Bertner Ave, Houston, TX 77030. Tel: (713) 792-3030.

Nov 14–15. **Cardiology Department Management Conference.** Dallas. Info: Lisa Krehbiel, The Institute for Medical Studies, 30131 Town Center Dr, Suite 215, Laguna Niguel, CA 92677. Tel: (714) 495-4499.

UTAH

Nov 14. **Basic Pulmonary Radiology.** 8 Cat 1 Credits. Salt Lake City. Info: Department of Education, LDS Hospital, Eighth Ave and C St, Salt Lake City, UT 84143.

AROUND THE WORLD

CANADA

Nov 12–14. **Sexuality and Health: A New Look at an Old Subject.** Edmonton, Alberta. Info: Chairman, Conference Planning Committee, Health Education and Promotion, Alberta Social Services and Community Health, Fifth Floor, Seventh St Plaza, 10030-107 St, Edmonton, Alberta, T5J 3E4. Tel: (403) 427-4680.

ISRAEL

Nov 2–9. **4th International Seminar on the Treatment of Rheumatic Diseases.** Tel Aviv. Info: The Secretariat, PO Box 394, 61 003 Tel Aviv, Israel.

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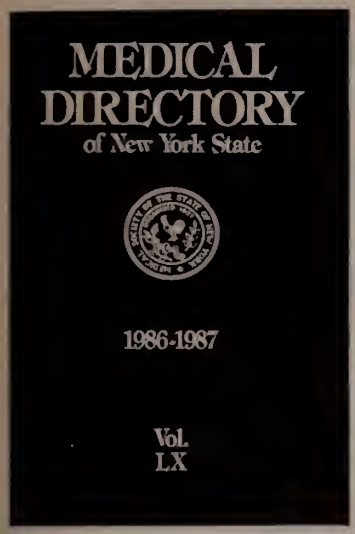

ANNOUNCING THE 1986-87 Edition of the MEDICAL DIRECTORY of New York State

Published, biennially, by the Medical Society of the State of New York, this important 920 page, reference source will be available in August 1986.

The Directory lists over 27,000 New York State physicians, both members of the Medical Society, and non-members who chose to be listed for a fee. It includes the following data.

- Cities, towns and counties in which the physicians practice
- Hospital affiliations, Fellowships, and Board certifications
- Medical School and date of graduation
- Up to three office addresses and telephone numbers
- Separate list of hospitals with medical staffs identified.

Of course, the Directory is distributed free to members of the State Medical Society who will automatically receive the Directory when published. A special price of $40 per copy is offered to non-member physicians who chose to be listed, and to all others the price is $70 per copy. The Directory is the most comprehensive, up-to-date desk reference source on physicians in New York State, and constantly utilized by physicians. libraries, and others in the health care field.

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★ **FINEBERG, Henry Irwin,** 420 Lakeville Rd 11042. Tel 488-6100. YALE 27. Am Thor. Am Pub Hlth, Ac Med. Exec Vice Pres Emerit Med Soc SNY. Also Dix Hills.

★ **LAWRENCE Jr, George J,** 420 Lakeville Rd 11042. Tel 488-6100. PENN 38. D-OG. SL. FACOG. FACS. Exec Vice Pres Emerit Med Soc SNY. Hon Chair O&G Flushing. Also Glen Cove (AMA)

★ **O'CONNOR, Robert James,** 33 Valencia Ave 10301. Tel 447-7242. STATE UNIV BKLN. D-OG SL. FACOG. FICS. Am Abdominal Sur. Am Ac Comp Med. Attd O&G Staten Isl. Cons O&G USPHSH SI. Attd Gyn Sea View. Also Lake Success. (MEM-AMA)

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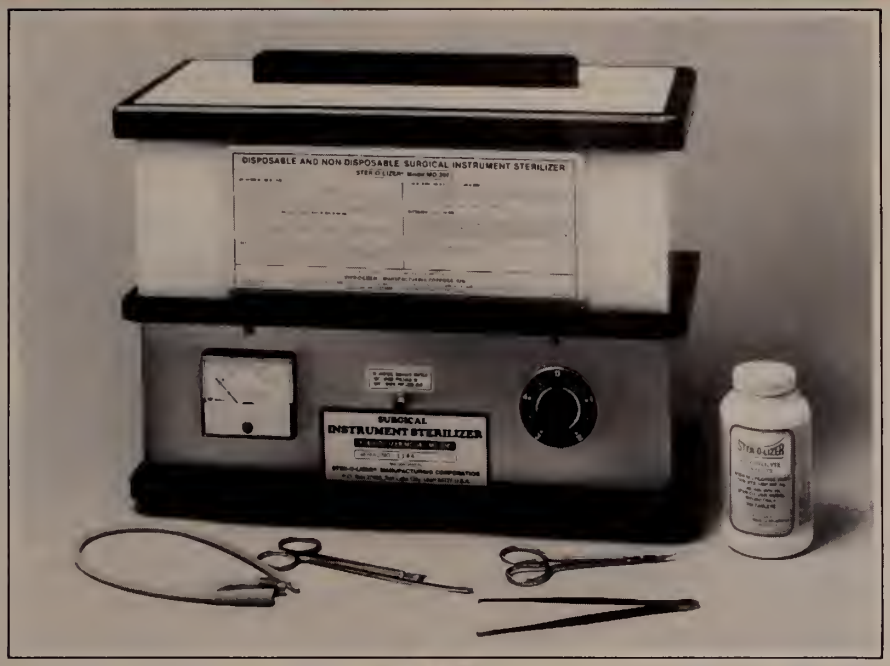

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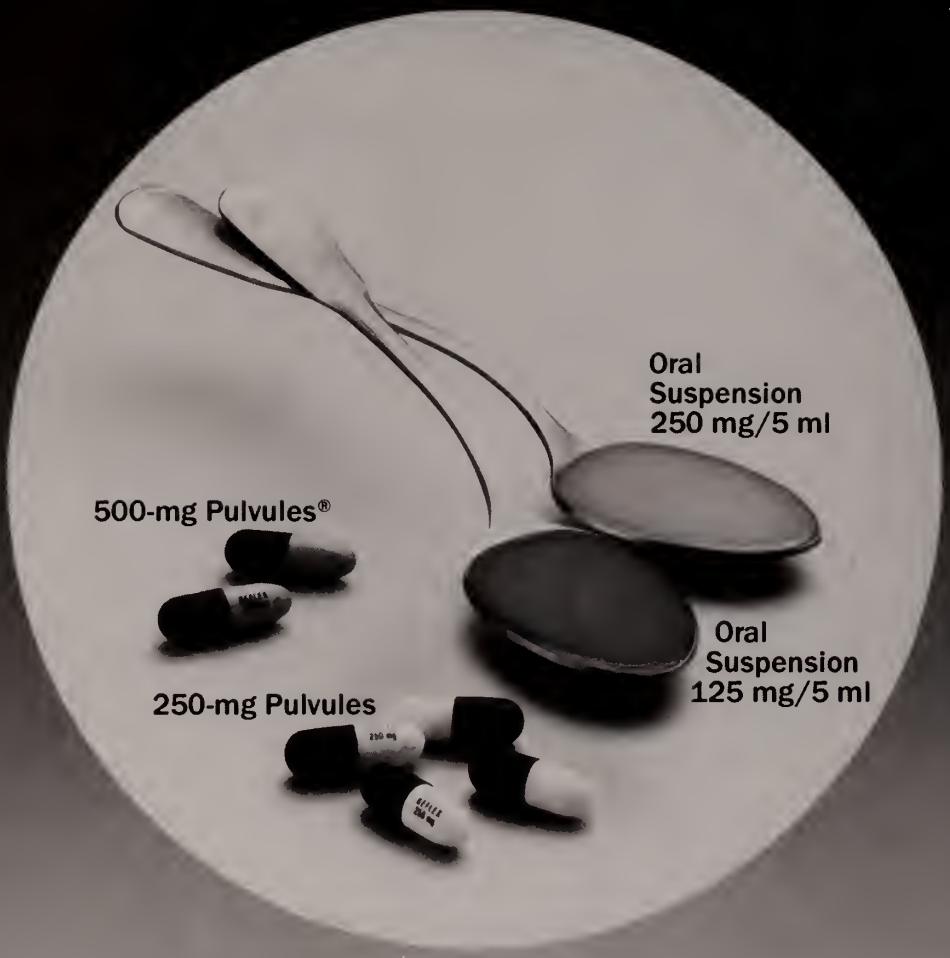

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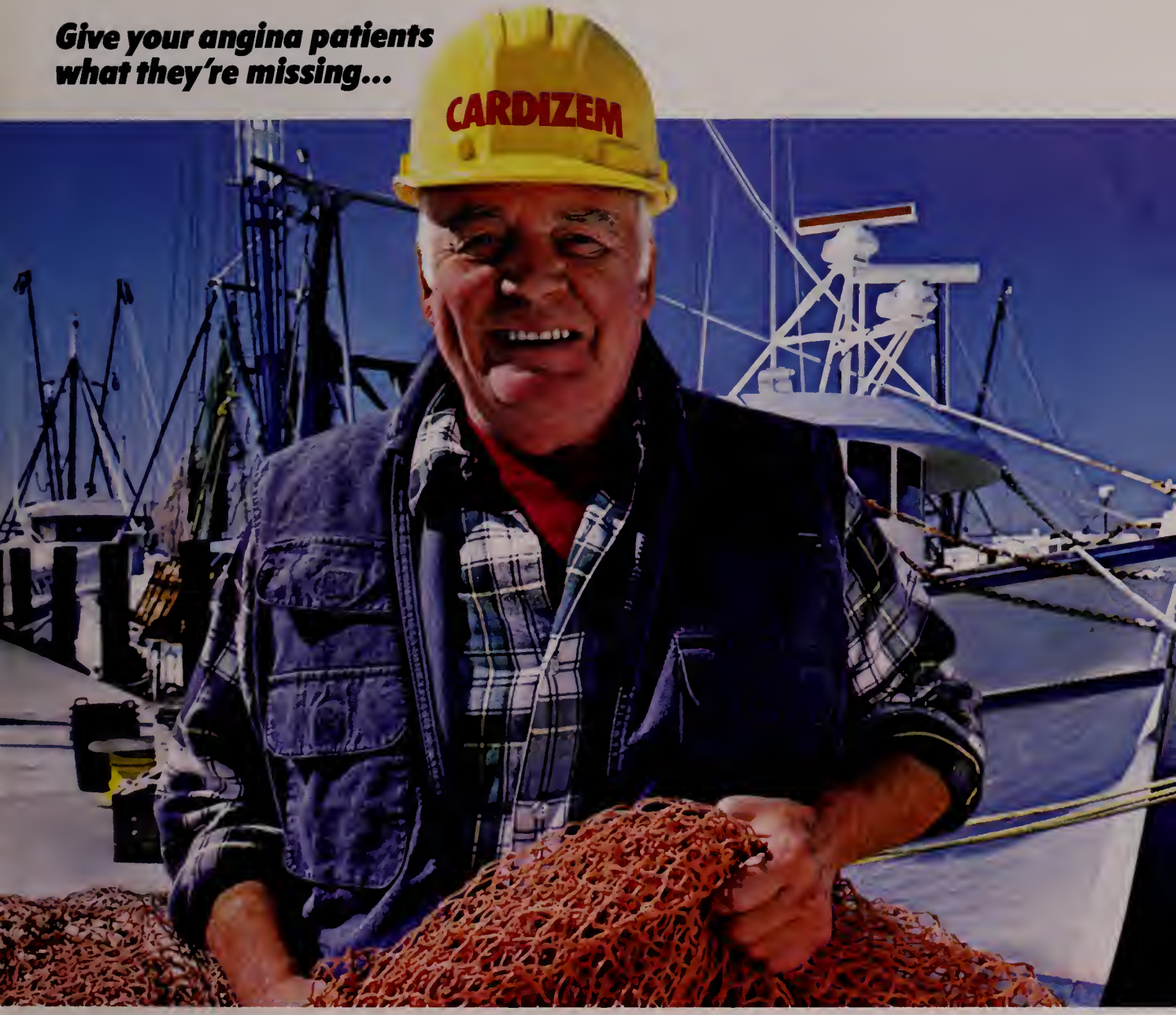

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CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. **Issued 7/86**

See complete Professional Use Information before prescribing.

References: 1. Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983, 106(6):1341-1347. **2.** Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984,24(Dec):150-159. **3.** Johnston DL, Lesawoy R, Human DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985;55:680-687. **4.** Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. **5.** Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982;50(Sept):94-116.

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MEETINGS AND LECTURES

The New York State Journal of Medicine *cannot guarantee publication of meeting and lecture notices unless the information is submitted at least three months prior to the event.*

DECEMBER 1986

AROUND THE STATE

MANHATTAN

Dec 4–5. **Current Topics in Gastroenterology & Nutrition—1986.** 16 Cat 1 Credits. College of Physicians & Surgeons of Columbia University. Info: Dr Elizabeth C. Gerst, Assistant Dean for Continuing Education, 630 West 168 St, New York, NY 10032. Tel: (212) 305-3682.

Dec 5–6. **Update on Male Impotence & Infertility for Urologists.** 14 Cat 1 Credits. NYU Medical Center. *Dec 8–10.* **Managing Clinical Problems in the Elderly.** 20½ Cat 1 Credits. NYU Medical Center. *Dec 8–11.* **Neurosurgery NYC/1986.** 22 Cat 1 Credits. Grand Hyatt New York. *Dec 15–20.* **Computed Tomography Head to Toe.** 38 Cat 1 Credits. Grand Hyatt New York. Info: NYU Medical Center Post-Graduate Medical School, 550 First Ave, New York, NY 10016. Tel: (212) 340-5295.

Dec 5–6. **Infection/Immunology in Obstetrics and Gynecology.** 12 Cat 1 Credits. The New York Hospital-Cornell Medical Center. Info: CRISIS, PO Box 4853, New York, NY 10185. Tel: (212) 696-0654.

Dec 6. **The Future of Cataract Surgery: Small Incision Surgery with Small Incision IOL's.** *Dec 13.* **Fluorescein and Laser Workshop.** Info: Martha Klapp, Manhattan Eye, Ear & Throat Hospital, 210 East 64 St, New York, NY 10021. Tel: (212) 605-3762.

Dec 6. **Hans Popper Symposium on Hepatitis: Clinical Cases, Pathology and Recent Advances.** 6 CME Credits. Mount Sinai School of Medicine. Info: Michael A. Gerber, MD, and Swan N. Thung, MD, Department of Pathology, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029. Tel: (718) 830-1981 or (212) 650-7732.

NASSAU

Dec 10. **A Clinical Day in Ophthalmology: Corneal Diseases and Keratorefractive Surgery.** 7 Cat 1 Credits. The Garden City Hotel. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Dec 10. **Nassau Surgical Society Day: Ophthalmology Section—Contemporary Ocular Therapy.** 4 Cat 1 Credits. Nassau County Medical Center Auditorium. Info: William Kasper, MD, Division of Ophthalmology/Department of Surgery, Nassau County Medical Center, East Meadow, NY 11554. Tel: (516) 542-2706.

WESTCHESTER

Dec 2. **Captopril and Its Use in Hypertension.** 1 Cat 1 Credit. *Dec 9.* **Hypertension—The Numbers Game.** 1 Cat 1 Credit. Nyack Hospital, Nyack. Info: Myrna Hahn, Nyack Hospital, N Midland Ave, Nyack, NY 10960. Tel: (914) 358-6200, ext 2509.

AROUND THE NATION

CALIFORNIA

Dec 1–5. **Doppler Echocardiography.** 43 Cat 1 Credits. San Francisco. Info: Kim Stroich, The Institute for Medical Studies, 30131 Town Center Dr, Suite #215, Laguna Niguel, CA 92677. Tel: (714) 495-4499.

Dec 11–12. **AIDS and the Nervous System.** 11 Cat 1 Credits. St Francis Hotel, San Francisco. *Dec 11–12.* **An Update in Neuro-Ophthalmology.** 13 Cat 1 Credits. Hyatt on Union Square, San Francisco. Info: University of California School of Medicine, Extended Programs in Medical Education, San Francisco, CA 94143. Tel: (415) 476-4251.

FLORIDA

Dec 3–7. **Ear, Nose and Throat Diseases in Children: A 1986 Update.** 17 Cat 1 Credits. The Breakers, Palm Beach. Info: Department of Otolaryngology, Children's Hospital of Pittsburgh, 125 De Soto St, Pittsburgh, PA 15213. Tel: (412) 647-6215.

ILLINOIS

Dec 4–6. **Advanced Colposcopy and Laser Surgery in Obstetrics and Gynecology.** 17½ Cat 1 Credits. Northwestern University Medical School, Chicago. *Dec 11–13.* 17 Cat 1 Credits. Hyatt Regency Hotel. Info: Paula Puntenney, Alumni Center for Continuing Education, Northwestern University Medical School, 301 East Chicago Ave, Chicago, IL 60611.

KENTUCKY

Dec 19–20. **Advances in Gastrointestinal Surgery.** Hyatt Regency Hotel, Lexington. Info: Joy Greene, Continuing Medical Education, 132 College of Medicine Office Building, University of Kentucky, Lexington, KY 40536-0086. Tel: (606) 233-5161.

AROUND THE WORLD

ENGLAND

Dec 11–13. **The Management and Financing of Hospital Services.** Barbican Centre for Arts and Conferences in London. Info: Dianne Cesaroni, Executive Programs, Yale School of Management, Box 1A, New Haven, CT 06520. Tel: (203) 436-0808.

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Medical Society of the State of New York

ANNUAL CME ASSEMBLY

Clinical Dilemmas & Controversies

March 13–15, 1987

and the

Annual Meeting of the House of Delegates

March 12–15, 1987

The New York Hilton
New York City

HIGHLIGHTS . . .

- 22 Sessions
- Panel Discussions
- Technical Exhibits
- Two Receptions
- President's Reception & Dinner Dance

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DEPARTURE DATE _____

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Annual Meeting of the House of Delegates
March 12–15, 1987
Annual CME Assembly
March 13–15, 1987

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GENERAL INFORMATION

All physicians, members of the allied professions, and their guests are invited to attend the Medical Society of the State of New York's Annual CME Assembly to be held March 13–15, 1987, at the New York Hilton. The two and one-half days of meetings will provide the individual physician with a possible 18 credits out of a total of 93 Category 1, CME credit hours being offered. The Medical Society of the State of New York is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for physicians. Over 125 outstanding speakers, including a number from out-of-state, will present papers at 20 sessions.

The theme of the CME Sessions will be "Clinical Dilemmas and Controversies." A few of the subjects to be presented will be, Terrorism & Medicine; Computers in Medicine; AIDS in Pregnancy; Humanism and Medical Ethics in Our Technological Age; Intensive Care for AIDS Victims; Thoracic Aortic Balloon Occlusion: Methods and Indications; and the Role of the Physician as the Patient's Advocate. For details, see the Preliminary Program which appears in the December 1986 issue of the *New York State Journal of Medicine*. Our program will offer the clinician timely approaches in diagnosis and treatment of diseases in a wide range of medical specialties.

Here are comments from some of the attendees at the 1986 CME Assembly: "The sessions were educational, and the topics were timely," "There was an excellent choice of qualified speakers," "I found the material was practical, concise and clinically useful." Don't miss this opportunity to gain category 1 credits over a weekend when you are free from office hours. Also, bring your family to New York City to enjoy the sights. There is no registration fee for MSSNY members or members of any other state medical society.

Professional representatives from more than 60 companies will be in the Rhinelander Gallery Exhibit Hall on Friday and Saturday to discuss their products and services. The Technical exhibits will include drug products, office management systems, medical and surgical suppliers, health insurance plans, pension plans and more.

SPECIAL EVENTS

Thursday, March 12

The Annual Dinner Dance, in honor of our President, John Finkbeiner, M.D., will be held in the Trianon Ballroom of the New York Hilton. The reception will be held in the Mercury Ballroom starting at 7:00 p.m. All attendees are welcome. Tickets are $75.00 per person and should be ordered in advance from the Medical Society.

UNITED NATIONS HEADQUARTERS
— Courtesy N.Y. Convention & Visitors Bureau

Friday, March 13 and Saturday, March 14

A reception for physicians, their guests, the allied professions and exhibitors will be held both days in the Exhibit Hall between 5:00 p.m. and 6:00 p.m. A free drawing for a color TV set will take place at both receptions.

HOTEL RESERVATIONS

Physicians must make their own reservations with the New York Hilton no later than February 19, 1987. After that date, rooms are on an availability basis only. If making reservations by telephone, please mention that you are attending the Medical Society Convention for billing at the special rate.

REGISTRATION

CME Registration will take place in the Exhibit Hall on Friday, March 13, from 8:00 a.m. to 5:30 p.m., and Saturday, March 14 from 8:30 a.m. to 5:30 p.m., and on Sunday, March 15, registration will take place on the 2nd floor Promenade from 8:30 a.m. to 12:30 p.m.

House of Delegates registration will take place on the 2nd and 3rd floor Promenades at the following hours: Wednesday, March 11, from 12 Noon to 6:00 p.m.; Thursday, March 12, Friday, March 13, and Saturday, March 14, from 8:30 a.m.–5:30 p.m.; and Sunday, March 15, from 8:30 a.m. to 12 Noon. All MSSNY members are invited to attend the meetings.

CME MEETING HOURS

Friday, March 13 —	9am – 12:30pm
	2pm – 5pm
Saturday, March 14	10am – 1pm
	2pm – 5pm
Sunday, March 15	10am – 1pm

EXHIBIT HOURS

Friday, March 13 —	9am – 6pm
Saturday, March 14	9am – 6pm

1987 ANNUAL CME ASSEMBLY

Medical Society of the State of New York
The New York Hilton, New York City

Clinical Dilemmas and Controversies

FRIDAY, MARCH 13

9:00 a.m. - 1:00 p.m. General Session: Clinical and Ethical Dilemmas, *Gramercy A & B*

2:00 p.m. - 5:00 p.m.
Chest Diseases, *Regent Parlor*
Cardiovascular Diseases, *Murray Hill B*
Pediatrics/Orthopedic Surgery, *Murray Hill A*
Neurology/Alcoholism/Physical Medicine & Rehabilitation, *Nassau A*
Emergency Medicine/Critical Care/Otolaryngology, *Gramercy B*
Medical Liability, *Gramercy A*

SATURDAY, MARCH 14

10:00 a.m. - 1:00 p.m.
Internal Medicine (All Day), *Regent Parlor*
Ophthalmology (All Day), *Sutton Parlor Center*
Psychiatry (All Day), *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation (All Day), *Murray Hill A*
Urology/Pathology, *Nassau A*
Dermatology, *Nassau B*

2:00 p.m. - 5:00 p.m.
Internal Medicine, *Regent Parlor*
Ophthalmology, *Sutton Parlor Center*
Psychiatry, *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation, *Murray Hill A*
Computers in Medicine, *Madison Suite*
Terrorism and Medicine, *Sutton Parlor South*

SUNDAY, MARCH 15

10:00 a.m. - 1:00 p.m.
Allergy and Immunology, *Murray Hill B*
General Surgery/Radiology/Anesthesiology, *Murray Hill A*
Obstetrics and Gynecology/Women's Medical Society of New York State, *Gramercy B*
Family Practice/Orthopedic Surgery, *Nassau A*
Neurosurgery, *Morgan Suite*

CME CREDITS: Each program will be eligible for CME Category 1 credits on an hour-for-hour basis. The Medical Society of the State of New York is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for physicians.

Technical Exhibits

The Brooklyn Bridge (foreground) and the Manhattan Bridge spanning the East River

Advance Registration Form

1987 Annual CME Assembly, March 13–15
The New York Hilton, New York City

Complete and return this form to the Medical Society address as indicated below.

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REGISTRATION FEE *Please check categories*

- ☐ Non-Member Physician* $50.00
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- ☐ Physician Assist.
- ☐ Dentist
- ☐ Lab Technician
- ☐ PT/OT
- ☐ Other_____ *Specify*

NO FEE *Please check category*

- ☐ Active Member*
- ☐ MSSNY Life Member
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- ☐ Medical Assist.
- ☐ Speaker
- ☐ Spouse/Family
- ☐ News Media/Medical Writer

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* of any state medical society

Please make check payable to:
Medical Society of the State of New York, and return this form with remittance to: Division of Meeting Services/MSSNY, 420 Lakeville Rd., P.O. Box 5404, Lake Success, N.Y. 11042.

Important: Your ID Badge will be held at the MSSNY Registration Desk located in the Exhibit Hall, on the second floor of the New York Hilton.

NEW YORK STATE
JOURNAL OF MEDICINE

November 1986 • Volume 86, Number 11

COMMENTARIES

Is balance billing doomed?

Massachusetts appears to be the "bellwether" state these days with respect to physician reimbursement. The Commonwealth State is battling the medical establishment and—worst of all—other states may join the fray.

The battle centers on physicians who charge more than the fees set by Medicare, which is legal in every state except Massachusetts, where a recently enacted law prohibits physicians from "balance billing." With balance billing, the patient is charged the difference between what Medicare allows and the physician's usual fee.

Although only 28% of physicians nationwide have signed Medicare participation agreements, some 73% of all Medicare claims are taken on assignment, which means that most Medicare beneficiaries incur no out-of-pocket expenses except their deductibles and co-payments.[1] This apparent discrepancy is caused by the fact that nearly three-fourths of the so-called "nonparticipating" physicians accept assignment on Medicare claims.

For their generosity, these nonparticipating physicians have been rewarded by Congress by having both their charges and their reimbursement levels frozen for the past two and a half years; they continue to be paid on the basis of their 1982 charges.

Originally, the goal of the Medicare participating physician program was to encourage more physicians to accept assignment. The best way to accomplish this, however, is to reimburse physicians equitably so they do not have to charge beneficiaries more than what Medicare determines to be the "reasonable" fee. Actually, Medicare reimburses physicians an average of 68% or less of their normal charges for most services.[1]

In 1985, physicians billed patients $2 billion over what Medicare reimbursement allowed. A patient's out-of-pocket expenses may total just a few dollars or as much as several thousand dollars. In some instances even a small additional charge can burden older, lower-income patients who require relatively frequent medical care.[2]

On the other hand, most physicians are sympathetic to such circumstances, but they do not feel they should have to grant the same discount to all senior citizens that they may grant to those who really need it by accepting assignment. Physicians should have the right to set different fees for different individuals with varying economic means.

The American Medical Association (AMA) has challenged the Massachusetts statute as being contrary to the intent of Congress. The linking of licensure to reimbursement under Medicare not only bears no relation to a physician's fitness to practice medicine but also would appear to be unconstitutional. What other conditions might be attached to licensure? The Massachusetts State Medical Society and the AMA lost in district court, but have appealed to a federal appeals court in Boston which will hear the case sometime this fall.

Proponents of the law note that Massachusetts has a similar law prohibiting physicians in the private Blue Shield insurance program from charging more than the program's rates. In April 1985, the United States Supreme Court let stand a lower court ruling that rejected physicians' arguments that Massachusetts Blue Shield was guilty of antitrust violations and price-fixing.[3]

A decision by the federal appeals court in Boston upholding the Medicare balance-billing prohibition would no doubt speed attempts to spread similar statutes around the country. What is most frightening is that legislators in several states are considering measures similar to the Massachusetts law which could strip physicians of their licenses if they bill patients more than the Medicare-approved rate.

For example, in Washington State, the Puget Sound Council of Senior Citizens is gathering signatures for a petition to force legislative consideration of a proposed balance-billing ban. A Rhode Island measure similar to the Massachusetts law died last year, but will come back. In California, state Senator Diane Watson is awaiting the outcome of the Massachusetts case before reintroducing similar legislation.

Although the Massachusetts law is not the solution for remedying the problems of the elderly with medical bills,

it is clear that physician reimbursement and particularly balance billing is being targeted by both lawmakers and consumer groups. Such groups are preparing to apply pressure on state legislatures to enact similar measures. There is no question that interest in the notion is growing all over the country, with a watchful eye being kept on the outcome of the present litigation in Massachusetts.

Fortunately, the Reagan administration, which has frozen physician fees under Medicare, has indicated it does not support mandatory measures against balance billing. William Roper, the administrator of the federal Health Care Financing Administration, and, like Secretary Otis Bowen, a physician, has indicated that federal officials are "strongly opposed" to further regulation of physicians. He fears that forcing them to accept only the set fee may lead many to refuse to see Medicare patients.

Furthermore, even the American Association of Retired Persons (AARP) is concerned that forcing physicians to accept only the Medicare payment could drive some away from caring for the elderly. The AARP supports bans on balance billing, but only if accompanied by a complete reevaluation of Medicare reimbursement.

DONALD F. FOY
Executive Vice-President
Medical Society of the
State of New York
Lake Success, NY 11042

1. A balanced approach to Medicare reimbursement [editorial]. *American Medical News*, September 12, 1986; 29(34):4.
2. *Constraining National Health Care Expenditures: Achieving Quality Care at an Affordable Cost*. General Accounting Office publication No. GAO/HRD-85-105. September 1985, p 187.
3. *Kartell v Blue Shield of Massachusetts, Inc*, 582 F Supp 734 (D Mass), *aff'd in part and rev'd in part*, 749 F2d 922 (1st Cir 1984), *cert denied*, 105 S Ct 2040 (1985).

Fifth disease and arthritis: Common immune-mediated responses to parvovirus infection

"My daughter's been sent home from school because of a bright red rash on her face," Melanie's mother told me. "I'm sure she didn't have it when she left for the bus stop, so this is something that's suddenly come on her. Melanie feels fine now and I want to send her back to class. What's happening, doctor?"

Melanie was an otherwise healthy nine-year-old sporting a rash from head to toe. Her face glowed with symmetrical malar erythema, sparing the bridge of the nose. Had someone just slapped both her checks? Melanie's trunk and extremities—including palms and soles—were covered with maculopapular lesions. The rash coalesced on her upper arms, in a pattern resembling lakes and rivers on a map.

I was in my second month as an Air Force pediatrician, having been drafted after my first year of pediatric residency. Each day I examined about 40 children from military families living in the vicinity of Wright-Patterson Air Force Base in Dayton, Ohio, but I had never seen a rash like this before. So I conferred with Dr Joel Steckelman, a keen and more experienced clinician. I suggested to him that the facial rash resembled systemic lupus erythematosus, but I doubted that diagnosis because Melanie did not have constitutional symptoms. Also, I remembered that the bridge of the nose was always involved in the "butterfly rash" of lupus. Joel recited a thorough differential diagnosis, concluding that Melanie most likely had fifth disease, also known as erythema infectiosum.

Thanking Joel for his assistance, I returned to my patient and her mother to explain the situation. I described the likely diagnosis as a relatively harmless, self-limited infection of unknown etiology. However, rubella was endemic in central Ohio at that time, and therefore I instructed Melanie's mother to keep her daughter home until the rash cleared, and to phone me daily to report on her daughter's progress.

After seeing my last patient of the day, I sequestered myself in the medical library to learn all that I could about fifth disease. I read that fifth disease is so named because the common childhood exanthems were numbered early in the 20th century. The first three (scarlet fever, rubeola, and rubella) had a well-defined etiology. The fourth, Filatov-Dukes disease, a curious variation of scarlet fever, had disappeared. Erythema infectiosum was "the fifth disease" and roseola infantum was "the sixth." I found an article by Wadlington[1] that neatly detailed the appearance and evolution of the rash. Melanie's case fit Wadlington's description perfectly!

Melanie remained well except for mild pain in her fingers and swelling of the dorsum of the hands and feet. The rash, aggravated by sunlight and exercise, waxed and waned for eight days and then disappeared. Melanie's experience with fifth disease was over but mine had just begun. Melanie represented the index case of a community-wide outbreak of erythema infectiosum involving 153 patients—an epidemic that launched my career in clinical virology.

Today, nearly two decades later, we could provide Melanie and her mother with more precise information about fifth disease. We now know that fifth disease is a common host response to acute human parvovirus infection.[2] Credit for that discovery goes to Mary J. Anderson and her colleagues[3] at King's College Hospital Medical School, London, who are also responsible for initiating the devel-

opment of a sensitive and specific diagnostic test. *Parvus* is Latin for small. Indeed, the virus is small, with a uniform diameter of 23 nm (about the size of poliovirus) and a molecular weight of 1.2–2.2 × 10^6 daltons. The single-stranded DNA genome is only big enough to code for one protein and serves as a template for its own replication.[4]

The history of human parvoviruses begins in the mid-1970s with the discovery by electron microscopy of parvovirus-like particles in blood and stool specimens. In 1975 parvovirus B19 was isolated from a unit of blood by Cossart et al[5] and at first was thought to be the elusive agent of non-A, non-B hepatitis. That notion was quickly disproved on sero-epidemiological grounds. Hints that fifth disease was caused by parvovirus B19 are found in a paper by Paver and Clarke[6] in 1976. These workers identified parvovirus particles in the serum of a blood donor whose four children "had itchy rashes" between three and a half and five weeks after she gave blood. Parenthetically, pruritus was present in nearly two thirds of our Ohio cases.[7,8] Paver and Clarke also wrote that one of the 11 viremic subjects reported by Cossart and her colleagues[5] developed a "rubelliform rash" four days after the viremia.

However, human parvovirus remained an agent in search of disease until 1981, when parvovirus B19 was serendipitously linked with aplastic crises in sickle cell anemia.[9] Because parvovirus B19 has a predilection for invading and destroying late erythroid progenitor cells of the bone marrow,[10] it triggers aplastic crises in patients with several forms of red blood cell abnormalities, including sickle cell anemia, pyruvate kinase deficiency, and hereditary spherocytosis.[11] Rarely, parvovirus causes hemolytic anemia in otherwise normal patients.[12] Two years after the association of parvovirus with aplastic crises was documented, the virus was shown to be the cause of fifth disease.

Parvoviruses can be acquired through transfusion of blood products[13] but the usual mode of transmission is via respiratory secretions. Serologic surveys show that the virus is most commonly encountered between the fourth and tenth years of life.[11] Parvovirus from human serum can infect susceptible volunteers when administered as nasal drops.[11] Viremia develops seven to eight days post inoculation and lasts as long as four days. One volunteer thus far has developed a rash, which occurred 16 days after nasal instillation of virus and eight days after cessation of viremia. In all studies to date, viremia has not been detected at the time of the rash. A skin biopsy of the rash from one of our patients showed perivascular lymphocytic infiltration.[8] These and other epidemiologic data suggest that fifth disease is an immune-mediated reaction occurring 14–17 days after primary parvovirus infection.

Arthritis is a common manifestation of many immune complex diseases. Not surprisingly, arthritis is the most common complication of fifth disease, as emphasized by Joseph,[14] whose article appears in this issue of the *Journal*. Adults with fifth disease can have joint involvement that mimics rheumatoid arthritis, and parvovirus arthritis can occur with or without the classic fifth disease rash.[15] Whether or not parvoviruses are a cause of chronic joint disease remains to be determined.

The only other significant but rare complication of parvovirus infection is encephalitis.[16,17] I believe that fifth disease encephalitis, like arthritis, is a postinfectious immune-mediated phenomenon.

One very perplexing question emerges from the rapidly evolving parvovirus saga. Is parvovirus harmful to the human fetus? One of Joseph's[14] patients, who contracted fifth disease during her fifth month of pregnancy, delivered an apparently normal infant. But recent letters in the *Lancet* implicate parvovirus as a cause of fetal damage.[18,19] Because parvoviruses prefer rapidly dividing cells, the human fetus could be a target for parvovirus invasion. In addition, veterinarians have long recognized that porcine parvovirus is a common cause of swine reproductive failure worldwide,[20] and a vaccine has been developed to combat this problem.

Most pediatricians, myself included, advise no isolation precautions for fifth disease. We would permit patients like Melanie to attend school. The present data are too scanty to warrant quarantine measures and, by the time the rash develops, patients are very unlikely to be contagious. However, a carefully planned prospective study with appropriate virologic monitoring is needed to determine if parvoviruses pose a risk during pregnancy. Such a study might convince us to change our minds about the need for isolation and could provide the rationale for development of a human parvovirus vaccine.

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Human parvovirus and fifth disease

What do spontaneous abortions, childhood rashes, adult arthritides, and aplastic crises of hereditary anemia have in common? Had the question been asked in 1984 it could not have been answered. But accumulating evidence now implicates a human parvovirus (HPV) in all of these conditions.

The prologue to the HPV story began almost a century ago when erythema infectiosum (fifth disease) was first distinguished from other rash diseases,[1] becoming familiar to generations of pediatricians as a benign childhood exanthem seen in springtime school outbreaks. Fifth disease became equally familiar to school and public health officials, who likewise considered it a harmless spring visitor. Cumulative data from many outbreak investigations suggested a single unknown virus, transmitted from person to person, that caused both apparent and inapparent cases, and that affected teachers and parents less frequently than schoolchildren, but more severely.[2]

The cause of fifth disease was still a mystery in 1980 when a seemingly unrelated discovery was made: Investigators screening children's sera found antibody to HPV in a single child.[3] This obscure orphan virus had been discovered in the sera of mostly healthy blood donors in France in 1972 and in England in 1975. But the patient tested in 1980, a ten-year-old boy with sickle cell disease, was suffering an aplastic crisis. Additional banked sera from other children with sickling crises were also found to be positive for HPV antigen or antibody, and evidence of HPV infection was found in the sera of all five children with paired specimens. Confirmation by other groups quickly followed, identifying HPV as a cause of aplastic crises in sickle cell disease, hereditary spherocytosis, beta-thalassemia intermedia, and pyruvate kinase deficiency. Studies suggested that the pathogenesis of aplastic crises in these patients involved erythroblastopenia due to a transient cytotoxic effect of HPV upon erythrocyte progenitor cells in the bone marrow,[4] an effect presumably masked in persons with a normal erythrocyte life span, but exposed in persons with shortened erythrocyte survival. Because persons with hereditary anemias have increased numbers of marrow erythroid precursors, it was suggested that their risk of serious HPV infection is also increased by the greater numbers of target cells susceptible to infection, causing greater viremia and spread to other cells.

Further information about HPV infection followed the development of sensitive radioimmunoassays for virus and for the detection of IgG and IgM; of HPV monoclonal antibodies; and of techniques for DNA hybridization. Aplastic crises were linked to antigenemia that disappeared with the appearance of antibody, and serum IgG and IgM antibodies were both shown to be useful in diagnosis. More surprisingly, serosurveys undertaken in several countries showed HPV infection to be common, with adult seroprevalence rates in the 60–65% range, and peaks of seroconversion in the middle childhood years.[5] Since most of the healthy adult population seemed to have been silently infected, and since aplastic crisis was the only specific illness to which HPV had been linked, it seemed in 1983 that HPV was of minor importance as a human pathogen. Then evidence from rheumatology clinics began to implicate HPV as a cause of sporadic acute arthritis, predominantly in adult women. Clinically, HPV-associated arthritis was described as symmetrical and polyarticular, beginning abruptly and resolving over several weeks. Later, persisting and relapsing cases were described, including some that met accepted criteria for adult rheumatoid arthritis, though usually lacking rheumatoid factor or antinuclear antibodies. To add to the confusion, in 1983 a parvovirus different from HPV was isolated from a patient with proven rheumatoid arthritis.[6] Since 1983, HPV has been linked to early spontaneous abortion with widespread infection of the fetus and fetal erythroblastosis. Also linked to HPV is a syndrome of "vascular purpura," some cases of which are indistinguishable from Henoch-Schönlein purpura.

But the most improbable association of all was made in 1983 by British investigators who showed that a school outbreak of fifth disease was caused by HPV.[7] Confirmation has since come from investigations of other current and past outbreaks of fifth disease, including an instance of simultaneous epidemics of fifth disease and aplastic crises linked to HPV.[8] The elusive cause of fifth disease thus appears to have been found.

Yet how can a virus as harmful as HPV—capable of causing abortions, arthritis, and aplastic crises—possibly be the cause of fifth disease, which has been recognized and studied by countless clinicians, epidemiologists, and other scientists for nearly 100 years? How can the same virus that has silently infected most persons around the world cause outbreaks in which 20–40% of children and adults have obvious fifth disease? Why do patients with HPV-associated illnesses like aplastic crises and arthritis rarely have fifth disease, or even rashes? Why, with few exceptions, have children with fifth disease not been found to have aplastic crises or acute anemias? Why have fifth disease-associated arthralgias, which are common in children, and in their parents and teachers, rarely been associated with severe or persistent arthritis? Why had fetal loss not been associated with fifth disease? Why are sporadic cases of fifth disease rarely recognized?

Without excluding the possibility of virulence differences in HPV strains, some of these paradoxical observations could be due to biases of observation and selection. The patients with hereditary anemias or arthritis, for example, have usually been seen in specialty clinics, whereas studies of fifth disease are usually based upon school outbreaks with sample sizes that may be too small to detect complications of low incidence. Also, such studies typically concentrate upon illness in children, perhaps missing complications like arthritis that are more frequent in adults. Although the lone published study of HPV infection of volunteers hints at a broad spectrum of illnesses, it is necessarily limited in scope.[9] In the absence of prospective studies, the approach taken by Dr Joseph[10] in an article in this issue of the *Journal* is helpful. By studying families from his practice with sporadically identified cases of fifth disease, he has found secondary household cases of fifth disease and of adult arthritis, extending our knowledge of sporadic community HPV infection in otherwise healthy persons. He has even identified a case in a pregnant woman, happily reporting that her baby is well at one year of age.

Undoubtedly, there is still much to be learned about HPV and the diseases with which it is associated. The next few years should provide more exciting discoveries in the HPV story. The implications may be far-reaching, especially as the association with chronic arthritis is explored more fully. HPV remains a fascinating mystery, the final chapter of which remains to be written.

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Fifth disease: The frequency of joint involvement in adults

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ABSTRACT. This paper describes 13 children and six adults with fifth disease. The cases occurred in eight families from six adjacent Long Island communities in the spring of 1985. All of the adults with fifth disease had arthritis or arthralgia. In four of the adults, the diagnosis of fifth disease was supported by antibody studies. Arthritis and arthralgia in adults have been reported with a frequency of 0% to 81% in the few reported outbreaks of fifth disease that affected adults. Two recent studies in the United Kingdom suggest that the occurrence of arthritis is frequently caused by human parvovirus infection. The high frequency of arthritis and arthralgia in the patients described here, the occurrence of these disorders in previous outbreaks, and the linking of human parvovirus with arthritis in studies in Great Britain suggest that human parvovirus may be a much more frequent cause of acute adult arthropathy than was previously thought.

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Fifth disease (erythema infectiosum) is a mild infection, primarily affecting children, characterized by bright red cheeks followed by a maculopapular or reticular rash on other parts of the body. There are usually few or no associated respiratory or constitutional symptoms. In the past 60 years, there have been more than 30 reports of outbreaks of fifth disease in schools, institutions, and communities in the United States.

The human parvovirus was first discovered by investigators in England,[1] France,[2] and Japan.[3] It was found as a particulate antigen in the sera of asymptomatic blood donors. Tests to determine the presence of human-parvovirus-specific IgM antibodies became available in England in 1982.[4] More recently, human parvovirus has been implicated as the cause of fifth disease;[5] as a major cause of hypoplastic crisis in sickle cell disease,[6,7] hereditary spherocytosis,[8] pyruvate kinase deficiency,[9] and other hemolytic anemias;[10] and as a cause of purpura.[11,12] Two reports[13,14] extended the clinical spectrum of human parvovirus infection to include asymptomatic infections and respiratory infections without rash, and another report[15] implicated human parvovirus in an acute arthritis without respiratory symptoms or rash.

The occurrence of arthritis and arthralgia in adults with fifth disease has been recognized since the report by Ager et al[16] in 1966. In the present report, 13 children and six adults from eight families were seen for fifth disease in a pediatric practice. The families were from six different neighboring communities, and the school-age children attended eight different schools. The six adults with fifth disease all had arthritis or arthralgia. In each of the four families in which the adult arthropathy occurred, the diagnosis of fifth disease caused by human parvovirus was supported by IgM antibody studies. The antibody studies were carried out by the Respiratory Virus Laboratory at the Centers for Disease Control, Atlanta, Ga, using an ELISA IgM antibody technique (personal communication from L. J. Anderson, MD, summer, 1985).

PATIENTS AND METHODS

Eleven of the 13 children had the characteristic cheek rash of fifth disease, followed in several days by a generalized maculopapular or reticular rash. Most of the children had few if any constitutional signs or symptoms. Two teenagers did not have cheek rashes, but generalized maculopapular rashes without symptoms developed 18 days after the characteristic cheek rash of their eight-year-old sister. None of the children had arthritis or arthralgia. The adults all presented with generalized maculopapular rashes and arthritis or arthralgia. None had the characteristic cheek rash seen in children.

One of the affected adults was a teacher in a local school. The nine school-age children attended eight different schools. In none of the schools was there an awareness of an outbreak of fifth disease, though occasional cases were noted.

Table I presents the number of children and adults in the eight families and the number with clinical fifth disease. It should be noted that 12 of 18 adults and six of 19 children in the involved families did not have symptomatic disease. They may not have been infected, they may have been infected previously, or they may have had asymptomatic infections. Antibody studies were not carried out on the 18 individuals without clinical symptoms. The time intervals between cases in the families with more than one case are also presented. Based on eight intervals, the incubation period, with the exception of one seven-day period, appeared to range from 13 to 18 days.

The four families described here include only those in which the six adult cases of fifth disease occurred.

Family 1. A four-year-old girl developed a bright red cheek rash on May 1, 1985. By May 3, the cheek rash had disappeared and a maculopapular rash extended over her arms, legs, and trunk. On April 24, the child's mother had consulted an internist because of the sudden onset of painful swelling of both her hands at the proximal interphalangeal joints as well as painful knees, associated with a 12-hour pruritic pink rash on her extremities. The pain improved during the next three days, but when the mother was seen with the daughter on May 3, the mother still had some swelling and tenderness of her hands. Her arthralgia

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TABLE I. Number of Cases and Time in Days Between Appearance of Fifth Disease in Index Cases and Contacts Among Members of Eight Families, 1985

Family Number	Residence	No. of Adults	No. of Adults with Fifth Disease	No. of Children	No. of Children with Fifth Disease	Days Between Index and Subsequent Cases
1	Oyster Bay	2	2	2	1	1,7
2	Muttontown	2	0	3	3	18,18
3a	Hicksville	2	0	2	2	45,16
3b	Syosset	2	2	0	0	14
4	Oyster Bay Cove	2	0	4	3	15,17
5	Syosset	2	1	2	1	3
6	Syosset	2	0	2	1	—
7	Westbury	2	1	2	1	13
8	Syosset	2	0	2	1	—
Total		18	6	19	13	

lasted one month. On April 25 the child's father had developed swelling of his fingers and ankles and a transient, one-day pink rash on his legs. He became free of all signs and symptoms within 48 hours. A blood specimen drawn on May 3 revealed that the child's mother had IgM antibodies to human parvovirus. The child's eight-year-old brother never developed clinical fifth disease.

Families 3a and 3b. A seven-year-old girl was seen on May 12 with a low fever and a rash of three days' duration that had started on her face and spread to her arms and legs. When asked about family members with a rash or arthritis, the child's mother mentioned that her sister and brother-in-law had had episodes of rashes and arthralgias two months before. On March 11, the sister, a hospital nurse, had developed joint pains involving her hands, feet, knees, and hips, associated with a maculopapular rash of the body excluding the face. She was five months into her first pregnancy. The whole episode lasted four days but was severe enough to warrant a visit to her obstetrician and internist. Laboratory studies were negative for rubella, hepatitis, and infectious mononucleosis. On March 25, the sister's husband developed a body rash and joint pains in his shoulders and legs. His symptoms disappeared in four days, but he had a recurrence of the rash and joint pains two to three weeks later. Blood drawn from the sister on May 14 showed IgM antibodies to human parvovirus. She delivered a normal infant on July 12. The brother of the seven-year-old girl developed typical fifth disease on May 25.

Family 5. A five-year-old girl developed typical fifth disease with onset of rash on May 28. Her mother, a teacher in the same school as the daughter, developed an itchy maculopapular rash on her legs on May 31. The next day, she experienced severe knee pains that lasted two days. An eight-year-old son never developed fifth disease. IgM human parvovirus antibodies were demonstrated in blood drawn from the mother on June 14.

Family 7. The mother of two children discovered a rash on her ankles on June 15. By the next day the rash had extended to her extremities, and she experienced severe aching and swelling of her fingers along with pains in her elbows and knees. When seen on June 17 (because her own physician did not have office hours that day), she had a maculopapular rash on her extremities, and the joint pains and swelling were mostly gone. Her 15-month-old son was seen with typical fifth disease on June 28. Her five-year-old son never developed clinical disease. IgM human parvovirus antibodies were detected in a blood sample drawn from the mother on June 17.

Discussion

It is common pediatric experience to see a few cases of fifth disease almost every year. Because of the reported association of human parvovirus and arthritis in adults,[15,17] special efforts were made to look for adult cases in families of children with fifth disease. Of the 19 cases of fifth disease, six were among adults. Each of the adults had a rash, but none had the characteristic cheek rash of fifth disease seen in children. All had either arthritis (three cases) or arthralgia (six cases). The arthropathy occurred in the fingers (four cases), knees (four cases), ankles (two cases), and in the elbows, shoulders, and hips in one case each. In general, the arthropathy was of short duration, lasting less than four days in four cases and from two to four weeks in the other two cases.

Table II lists reports in the United States and British literature of fifth disease or human parvovirus infection involving five or more adults. Reports 1–5[16,18–21] are clinical reports of outbreaks of fifth disease. Reports 6–12[5,10,14,15,17,22] involve patients with proven human parvovirus infections. The small number of reports of fifth disease or human parvovirus infection affecting adults is striking. In seven of the 12 reports listed in Table II, some of the affected adults had either arthritis or arthralgia. It is possible that if arthritis or arthralgia had been looked for more intensively in the other five reports, these disorders may have been found in the adults. The clinical description of the cases in the report by Plummer et al[14] (in which none of the 17 children had the characteristic cheek rash and in which one of the seven adults had arthritis or arthralgia) differs markedly from the clinical picture seen here and in most other reports of outbreaks. The data are consistent with human parvovirus strain heterogeneity. From the data in Table II, it is not clear whether there are arthritogenic and nonarthritogenic strains of human parvovirus.

Two recent reports from Great Britain[15,17] suggest that human parvovirus arthritis, synovitis, and arthralgia of adults are common. The report by Reid et al[15] describes human parvovirus infection in 27 adults and three children, all with arthritis. All had symmetrical involvement of the small joints of the hands. The joints most commonly involved were: proximal interphalangeal (19 persons), metacarpophalangeal (14 persons), knees (14 persons), wrists (10 persons), and ankles (10 persons). In all patients, the arthritis was associated with significant stiffness, and in many cases the arthritis was severe enough to warrant absence from work. In 70% of patients the arthritis resolved within two weeks. A rash was present in only half of the adults, and seven adults had neither rash nor viral prodome. The report by White et al[17] describes 19 patients with arthritis with serologic evidence of human parvovirus infection. The 19 patients represented 12% of

TABLE II. Summary of Reports in the Literature with Five or More Adult Cases of Fifth Disease or Human Parvovirus Infection

No.	Author	Reference	Year of Occurrence	Geographic Location	No. of Children	No. of Adults	% Adults with Arthritis	% Adults with Arthralgia
1	Zuckerman	18	1938	California	122	6	0	0
2	Greenwald & Bashe	19	1963	Ohio	170	30	0	0
3	Ager et al	16	1966	Washington	307	57	60	77
4	Balfour	20	1969	Ohio	82	9	22	67
5	Edelson & Altman	21	1970	New Jersey	1,675	5	0	0
6	White et al	17	1979	England	0	19	95	100
7	Plummer et al	14	1980	Canada	17	7	0	0
8	Rao et al	10	1980	Illinois	—	7	0	0
9	Anderson et al	5	1983	England	33	6	0	33
10	Anderson et al	22	1983	England	195	20	—	81
11	Reid et al	15	1984	Scotland	3	27	100	100
12	Joseph		1985	New York	13	6	50	100

153 patients attending an early synovitis clinic. All were women over the age of 18 years. Eighteen presented with an acute, moderately severe, symmetrical peripheral polyarthritis. The joints involved were similar to the ones in the report by Reid et al.[15] In 17 cases the symptoms persisted for more than two weeks, and in three cases they persisted for more than four years. Ager et al[16] reported on 57 adult cases (patients more than 20 years of age) among a total group of 364 well studied cases in a community outbreak of fifth disease in Port Angeles, Washington, in 1961. Seventy-seven percent of the adults had arthralgia and 60% had arthritis. The arthritis was confined to the large joints of the extremities, particularly the wrist and the knee. The duration of arthritis was not described. In Balfour's report[20] of an epidemic of fifth disease in Ohio in 1969, nine adults were described among the 91 cases; four had arthralgia and two had arthritis. The average duration of arthropathy was three days, and the small joints of the hands were involved in all cases.

Nunoue et al[13] described a 1980–1981 outbreak of human parvovirus infection in a Japanese city. The authors carried out IgG antibody studies on a group of 780 hospital patients. The results suggest that in one Japanese city the prevalence of human parvovirus antibodies at age 20 is approximately 20%, and by age 70 it is over 50%. If the results are at all representative of the US population, they would suggest that 30% of adults in the United States become infected with human parvovirus at some time during adulthood. Assuming a total US population of 250 million, this would translate into approximately 75 million adult human parvovirus infections over 50 years, or approximately 1.5 million adult human parvovirus infections each year. On the basis of current information, these infections may be asymptomatic,[13] or they may occur as a respiratory infection with or without a rash and with or without arthritis or arthralgia, as a respiratory infection with petechiae and purpura,[11,12] or as arthritis alone.[15]

In this report, 25% of the adults (the adults in family 3b are excluded) developed an arthropathy. A number of reports, including this one,[15-17,20] in conjunction with the study by Nunoue et al[13] in Japan, suggest that human parvovirus infection is a more common cause of acute transient arthropathy in adults than had been thought. White et al[17] reported three cases in which arthritis lasted more than four years. This suggests a role for human parvovirus in chronic arthritis.

Anderson et al[23] provide interesting data in their paper on experimental parvovirus infection in human volunteers. In that experiment, nine human volunteers aged 45–52 years received intranasal inoculation with a dilution of plasma known to contain human parvovirus. Approximately one week after the inoculation a viremia was observed in five volunteers. Mild symptoms of pyrexia, malaise, myalgia, and itching were observed at that time in seven of the nine volunteers. Fourteen to 18 days after inoculation a second phase of illness was observed in five of the nine volunteers; this phase was characterized by an erythematous rash of the extremities, and arthralgia and arthritis of the hands, knees, and ankles. The rashes and arthropathy disappeared within a week. The second phase of illness was similar to the fifth disease illness in adults described in this paper and in the other reports listed in Table II.

One additional point of interest is the case of the woman in whom human parvovirus infection developed during the fifth month of pregnancy (Family 3b). The child of that pregnancy is now one year old, is healthy, and is demonstrating normal development. The data on outcome of pregnancies during which human parvovirus infections occur are just beginning to appear in the literature. The results of studies in Great Britain and France are summarized in two recent papers.[24,25] Of 20 pregnancies associated with human parvovirus infection, there were 13 healthy children born, five abortions, and two abortions with hydrops fetalis. The data on teratogenicity of human parvovirus are preliminary and inadequate, though one report 20 years ago by Ager et al[16]—based on data obtained without the benefit of antibody studies—suggested that the agent of fifth disease was probably nonteratogenic.

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See also pp 556-557 and 558-559.

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DIFFERENTIAL DIAGNOSIS OF THE EXANTHEMATA

SUMMARY.—We must consider these diseases separately.

We will first consider scarlet fever:

Scarlet fever presents cardinal symptoms. They are fever; sore throat or enanthem; skin eruption or exanthem. The fever and sore throat invariably appear at least twenty-four hours before the exanthem. The absence of any one of these cardinal symptoms precludes the possibility of scarlet fever. "Sine eruptione" cases undoubtedly do occur, but they must not be diagnosed as scarlet fever.

Equally important with the above symptoms are the rate of progress and duration of symptoms. Any throat affection and any skin affection due to scarlet fever virus will invariably persist to the second and even the third day after date of appearance.

In distinguishing scarlet fever from other conditions, we have to deal with simulations and dissimulations, with resemblances and differences.

Scarlet fever when present is usually recognized as such. When recognition fails, it is due to mildness or irregularity of symptoms. At its mildest the rate of progress and duration of the onset symptoms is comparatively constant.

The alien conditions simulating scarlet fever are many. Any of the other exanthemata may give a prodromal scarletina rash. Any infectious disease may give a scarletina rash. Sepsis gives the closest imitation; septic diphtheria, puerperal sepsis, sepsis accompanying burns are examples.

Many articles of diet may produce scarletinal rashes.

Many drugs give rise to skin conditions resembling scarlet fever.

Bearing in mind the order of appearance, the rate of progress, and the duration of symptoms in scarlet fever, we will find that all these alien conditions show divergences from the required syndrome within twenty-four hours.

In connection with smallpox, the diseases most frequently causing confusion in diagnosis are syphilis and varicella. Syphilis works much more slowly and varicella much more quickly than smallpox. Neither of these diseases produces umbilication in progressive lesions. The umbilication of smallpox lesions is pathognomonic. Again, the four day prodromal period of smallpox, with entire intermission of symptoms on appearance of rash, is foreign to both of these diseases.

One modification of smallpox, called alastrim, deserves notice. The prodromal period is prolonged to possibly five or six days. The initial rash consists of many, closely set, pinhead size pustules. These lesions come out as pustules and remain so without increase in size for several days. They do not progress and become characteristic smallpox lesions but desiccate without further development. These minute pustules are never generally distributed but appear in one or more patches on face, trunk or extremities.

WILLIAM L. SOMERSET, MD
(*NY State J Med* 1924; 24:617)

Polycythemia rubra vera

Case Presentation

Susan Y. Urban, MD (Medical Intern): A 71-year-old Philippine woman was admitted to the hospital because of swelling of the right calf for two weeks.

During the preceding five to six months, the patient had noted a ruddy complexion, injected conjunctivae, occasional blurred vision, occasional headaches, occasional palpitations, and a five-pound weight loss.

Two weeks prior to admission, she noted swelling, redness, and pain in her right calf, which got worse on standing up or walking; her physician advised hospital admission. She denied dyspnea, cough, or chest pain.

Ten years earlier, the patient had been treated for pulmonary tuberculosis with rifampin and streptomycin. A goiter had been present for five to six years, but had never been evaluated. She denied any history suggestive of chronic lung disease. Her medical history was not otherwise significant. Her only medications were multivitamins with iron. She had never smoked cigarettes or drunk alcoholic beverages. She experienced occasional pruritus that may have increased after a hot shower or bath.

The physical examination on admission revealed a well-developed, well-nourished woman with plethoric facies, who appeared younger than her stated age of 71 years. The blood pressure was 150/90 mm Hg; pulse rate, 128/min, with a regular rhythm; respiratory rate, 20/min and unlabored; temperature, 98.0° F by mouth. The palms and nail beds were erythematous. The skin was warm and moist, without cyanosis. The conjunctivae were markedly injected. Extraocular movements showed no lidlag. Funduscopic findings were normal. The mucous membranes of the mouth and oropharynx were injected. The thyroid gland was enlarged, soft, and nontender; a 3 × 3-cm firm nodule was present in the right lobe; no bruit was audible. A few rales were audible at the base of the left lung. The cardiac rate was rapid at 128/min; the rhythm was regular. The second pulmonic sound was very loud, and an S4 gallop was present. The abdomen was soft and nontender, without hepatosplenomegaly or masses. The rectal examination disclosed no abnormalities. The stool was negative for blood on guaiac test. The right calf showed diffuse rubor and increased warmth, swelling, and tenderness; no palpable cords or Homan's sign were evident. The patient's neurologic status was normal.

The urine was clear and yellow, with a pH of 6.0 and a specific gravity of 1.010. A dipstick test showed only a 1+ positive test for blood. The microscopic examination was negative. Subsequent urinalysis revealed mild hematuria.

The hemoglobin count was 22.5 g/dL, and the hematocrit was 72.4%. The white blood cell count was 21,400/μL with 83% polymorphonuclear leukocytes, 3% band forms, 9% lymphocytes, 1% eosinophils, 2% monocytes, and 2% basophils. The platelet count was 197,000/μL. The peripheral blood smear showed increased numbers of red blood cells with normal morphologic appearance. The erythrocyte sedimentation rate (ESR) was 2 mm/hr.

The initial and repeated prothrombin time (PT) was 27.4 sec (control, 12.0 sec); the initial and repeated partial thromboplastin time (PTT) was greater than 100 sec (control, 25.9 sec). After a 1:1 dilution of the patient's blood sample with normal plasma, the PT was 14 sec (control, 12 sec), and the PTT was 49 sec (control, 25.9 sec).

The leukocyte alkaline phosphatase level was 170 units (normal range, 11–95 U); the serum muramidase level was 18 μg/μL (normal range, 2.3–8 μg/μL). The lactate dehydrogenase level was 273 U/L (normal range, 91–180 U/L). The serum alkaline phosphatase level was 213 U/L (normal range, 13–39 U/L). The serum vitamin B_{12} level was 1,466 pg/μL (normal range, 171–953 pg/μL). The serum electrolyte levels, blood urea nitrogen (BUN), serum creatinine, uric acid, and blood glucose levels were within normal limits. The serum levels of T4, T3, and thyroid stimulating hormone (TSH) were normal. Arterial blood gas determinations with the patient breathing room air were as follows: pH, 7.43; P_{CO_2}, 38 mm Hg; P_{O_2}, 78 mm Hg; and bicarbonate, 25 mosm/L, with 95% oxygen saturation of hemoglobin.

An electrocardiogram revealed a sinus tachycardia of 114/min, with indication of right atrial enlargement, and left ventricular hypertrophy by voltage.

The initial diagnostic impression was deep vein thrombosis. The patient's state of hydration was improved with intravenous fluids. Blood and urine cultures were obtained, and oxacillin was administered intravenously. A venogram of the right leg was obtained, and the patient was started on heparin intravenously. When blood cultures were reported to be negative for bacterial growth, the oxacillin was discontinued.

A bone marrow biopsy revealed an extremely cellular marrow, a marked increase in all cell lines, and normal cell maturation—findings consistent with a myeloproliferative disorder such as polycythemia vera.

Based on a clinical conference held at the New York Infirmary, Beekman Downtown Hospital, New York City, on April 11, 1986.

Editor: JOHN T. FLYNN, MD.

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FIGURE 1. Posteroanterior chest film taken on admission showing chronic changes at lung bases, borderline cardiac enlargement, and displacement of trachea to right by enlarged thyroid.

FIGURE 2. Left lateral chest film taken on admission showing chronic changes at lung bases.

With removal of about 500 cc of blood every other day, the patient's hematocrit currently is 56%.

George Braff, MD (Director of Radiology): The posterior-anterior and lateral chest films showed chronic changes at the lung bases, with borderline enlargement of the heart (Figs 1, 2). The trachea was slightly shifted to the right, with considerable soft tissue mass effect in the lower cervical area, compatible with thyroid enlargement.

Venography of the leg, with injection of contrast material into veins of the foot, should show all of the material entering the deep venous system—that is, into the superficial femoral vein at the level of the knee. The venogram of the right leg in this patient showed cut-offs and "ghosts," or tram-track lines, which means that there is thrombus within the vessel itself. This was seen in the greater saphenous system, which also enters the deep system. The superficial femoral vein was completely occluded.

The liver-spleen scan was negative. A computed tomographic (CT) scan of the abdomen demonstrated a lesion on the lateral aspect of the mid-portion of the left kidney (Fig 3). The pancreas appeared normal. The left adrenal gland had a slightly bulbous appearance; a small adrenal adenoma or other mass could not be excluded.

Ultrasonography of the left kidney showed a multiocular cystic lesion which was benign in appearance (Fig 4). But, if a slight irregularity of the cyst wall can be identified, a small neoplastic lesion within the cyst cannot be ruled out.

Ultrasonography of the thyroid showed an enlarged gland with areas of increased and decreased attenuation. A technetium study of the gland showed discrete areas of increased uptake, with decreased uptake over the left lower lobe and in the right mid-portion of the gland (Fig 5). This appearance is consistent with multinodular goiter.

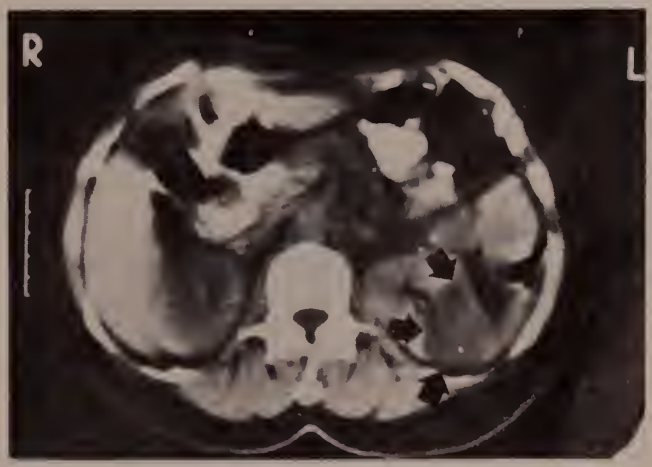

FIGURE 3. CT scan of abdomen showing cystic lesion on lateral aspect of left kidney (arrows).

FIGURE 4. Ultrasonograph of left kidney showing solitary cyst on lateral aspect of upper pole.

An I^{125} thyroid scan would help to demonstrate any areas of increased uptake and perhaps cold areas as well.

Richard Slubowski, MD (Medical Resident): Dr Urban, how did you account for the initially abnormal coagulation profile?

Dr Urban: In the blue-topped specimen tube for these tests, a total of about 3 cc of the patient's blood is customarily added to the anticoagulant already in the tube. With such a high hematocrit, three cc of this patient's blood would include only a relatively small amount of plasma and, therefore, a smaller than usual amount of plasma coagulation factors. So the amount of anticoagulant already in the tube would in fact be excessive. The prolonged coagulation times are artifactual errors that one would get even if one put too small an amount of a healthy person's blood into this tube.

FIGURE 5. Technitium-99 scan of thyroid showing irregular uptake indicative of multinodular goiter.

The Differential Diagnosis

Doris Lin, MD (Medical Resident): In erythrocytosis, the total body red cell mass can be determined with the aid of red cells labeled with chromium 51; the plasma mass can be determined using 125-iodinated albumin.

With hematocrit values of 70% or less, erythrocytosis can be either relative or absolute. A relative erythrocytosis involves a normal total red cell mass and decreased total plasma volume; it can occur with dehydration, severe burns, stress, smoking, increased alcohol intake, diuretic use, and endocrine disorders such as pheochromocytoma and Cushing's syndrome. Stress polycythemia, or Gaisböck's syndrome, is also a relative erythrocytosis which occurs most commonly in obese, anxious, middle-aged men, and is associated with thromboembolism, hypercholesterolemia, hyperuricemia, and angina pectoris. It is four times more common than polycythemia vera, and should not be treated with phlebotomy or chemotherapy, as is done in polycythemia vera.

This patient, with a hematocrit of 72%, had an absolute erythrocytosis. This involves an increase in total body red cell mass and a plasma volume that may be normal, increased, or decreased. In primary absolute erythrocytosis, erythropoietin levels in plasma or urine are low or absent;[1] in the secondary form, increased production of erythropoietin causes an increase in red blood cell (RBC) mass.

Erythropoietin is a hormone whose production is stimulated by oxygen sensors in the kidney.[2] The released erythropoietin causes increased red blood cell production in the bone marrow.

Physiologic increases in erythropoietin production and in hematocrit are seen in many persons who travel at 14,000 feet or more above sea level. Such increases occur in patients with chronic obstructive lung disease, when the arterial P_{O_2} falls below 65 mm Hg of oxygen tension, or when the oxygen saturation of hemoglobin falls below 92%.[2] Patients with congenital heart disease with a right-to-left shunt often have extreme erythrocytosis. Adults with acquired heart disease and chronic cardiac decompensation have reduced oxygen transport, but the increased RBC mass is obscured by an increase in plasma volume.

Another mechanism of increased red blood cell formation is the autonomous production of erythropoietin by certain tumors.[3] One third of such neoplasms are hypernephromas; the remainder include hepatomas, uterine leiomyomas, cerebellar hemangiomas, endocrine tumors with Cushing's syndrome, and pheochromocytoma.

Secondary erythrocytosis can occur as a result of defective oxygen transport. An altered affinity of the hemoglobin molecule for oxygen can cause an increase in RBC mass, as is seen in patients with low levels of RBC 2,3-diphosphoglycerate or methemoglobinemia, or in cigarette smokers with carboxyhemoglobinemia.

A nonphysiologic increase in erythropoietin production may occur in polycystic kidney disease and with multiple renal cysts.[2] Pressure on the remaining tissue may cause local renal tissue hypoxia, which can trigger increased erythropoietin production. Solitary renal cysts have not been described as a cause of secondary erythrocytosis.

The patient described here meets the classic criteria of primary erythrocytosis, that is, polycythemia rubra vera.

In 1968, the Polycythemia Vera Study Group adopted two groupings of criteria for this disease,[4,5] as indicated below:

Group 1

- RBC mass equal to or greater than 36 mL/kg of body weight in men and 32 mL/kg in women
- arterial oxygen saturation equal to or greater than 92%
- splenomegaly

Group 2

- thrombocytosis: platelet count greater than 400,000/μL
- leucocytosis of more than 12,000/μL in the absence of fever or infection
- increased leukocyte alkaline phosphatase: greater than 100 units in the absence of fever or infection
- serum vitamin B_{12} greater than 900 pg/μL, or unbound B_{12} binding capacity greater than 2,200 pg/μl

The diagnosis of polycythemia vera is made if the following combinations occur: all three parameters in Group 1 are present; or a combination of the first two parameters in Group 1 together with any two parameters from Group 2 is present. A diagnostic problem may occur when a patient with chronic lung disease is also in an early stage of polycythemia vera, before the development of splenomegaly or panmyelosis.

This patient satisfied the criteria of increased RBC mass, oxygen saturation of 95%, leucocytosis, increased leukocyte alkaline phosphatase, and an elevated vitamin B_{12} level. She also had an increased RBC count, with a hematocrit above 70%, and normal red blood cell morphology. Her bone marrow was hypercellular, with an increase in all cell lines, normal maturation, and absence of iron deposits—all compatible with a myeloproliferative disease. Cellularity occupying more than 75% of the marrow, together with an increased RBC count, strongly suggest the diagnosis of polycythemia vera.

Approximately one third of patients with polycythemia vera will have thromboses or hemorrhagic events during the course of the disease.[5] The risk of thrombosis is increased by accelerated atherosclerosis in the peripheral, cerebral, and coronary arteries of these patients. Patients with secondary polycythemia are less prone to peripheral vascular complications, except those patients with congenital heart disease.

Initially, this patient's tachycardia and her diffuse multinodular thyroid gland raised the possibility of toxic goiter. Thyroid hormone may stimulate red blood cell production indirectly by increasing cellular oxygen demand; treatment of the thyrotoxicosis corrects this erythrocytosis. However, results of thyroid studies were normal.

Review of Polycythemia Rubra Vera

James Malcolmson, MD (Medical Resident): Polycythemia vera is a neoplastic disease of late middle life; the incidence is about 0.6–1.8 per 100,000 of the general population. The onset is often asymptomatic, and the course is gradually progressive. The average survival time without therapy is no more than two years; with therapy, the median survival time is extended to 10–12 years.

The condition is due to neoplastic change in a single pluripotential marrow stem cell.[6] The resulting clone of cells from this one cell includes excessive numbers of red cells, granulocytes, and platelets, despite a decrease in serum erythropoietin. In other polycythemias, the white blood cells and platelets are not increased, and erythropoietin production is normal or elevated.

Headache, tinnitus, lightheadedness, vertigo, and blurred vision result principally from increased blood viscosity and hypervolemia. Thrombotic complications may involve both the venous and the arterial systems. Epistaxes, spontaneous bruising, and upper gastrointestinal hemorrhages have been attributed to hypervolemia and platelet dysfunction.

The increased incidence of peptic ulcer disease and pruritus in polycythemia vera may be related to the excessive histamine release caused by the rapid turnover of granulocytes, specifically the basophils. Characteristically, the pruritus is provoked by a hot bath or shower. Complaints of sweating and weight loss are presumably due to the hypermetabolic state. The cellular proliferation results in overproduction of uric acid, sometimes causing uric acid stones, or secondary gout.

The patient appears plethoric or cyanotic over the face, hands, feet, and mucous membranes; engorgement of the conjunctivae and retinal veins and occasional retinal hemorrhages are seen. Ecchymoses are frequent. Splenomegaly is important in the differential diagnosis, since it reflects the development of extramedullary hematopoiesis and is present in approximately 75% of patients with polycythemia vera.

The most prominent laboratory findings in polycythemia vera are the elevated hemoglobin level and increased red cell mass. Unless altered by iron deficiency, the red cells are normochromic; polychromasia is seen frequently. The red cells are usually normocytic, except in the later stages, when teardrop-shaped and nucleated red blood cells may be released from fibrosed marrow or from extramedullary sites. The erythrocyte sedimentation rate is frequently very low, as in this patient.

In about 50% of these patients, the white cell count rises above 12,000/μL, and sometimes to 60,000/μL. About 75% of patients also have an absolute basophil count greater than 65/μL, and more than 80% have an increase in the leucocyte alkaline phosphatase level. Increased granulocyte turnover is reflected by high serum and urine muramidase (lysozyme) levels. There are also increases in serum vitamin B_{12} and levels of transcobalamine-I and transcobalamine-III, with a resulting increase in unbound B_{12} binding capacity. The latter correlates well with disease activity and with effectiveness of therapeutic control.

In approximately 50% of patients, the platelet count may exceed 500,000/μL at the time of diagnosis and tends to increase with time, particularly with repeated phlebotomy. Some patients have abnormal platelet function, including that of platelet aggregation. A prolonged bleeding time may be present. The prothrombin time, the partial thromboplastin time, and fibrinogen levels are usually normal, when measured with the precautions mentioned by Dr Urban.

Bone marrow studies typically reveal hyperplasia, affecting all three cell lines; the myeloid-erythroid ratio in the marrow may be normal. Bone marrow biopsy, together with aspiration, allows a better assessment of the hypercellularity, and connective tissue stains illustrate the extent of myelofibrosis. Stainable marrow iron is decreased or absent in the majority of cases, presumably due to occult blood loss and to the intense utilization of iron during the expansion of red cell mass.

Some authorities suggest that when cellular elements occupy more than 75% of the marrow space, other investigations are not needed in order to exclude secondary erythrocytosis.

Inadequate control of red cell mass predisposes the patients to cerebral, vascular, coronary, and abdominal thrombotic occlusions, both arterial and venous. Thrombosis is the major cause of death in approximately one third of all fatalities in this disease; acute leukemia, hemorrhage, and myelofibrosis, collectively with thrombosis, account for 75% of all deaths. Acute leukemia occurs in 2–4% of patients, even without exposure to either radiotherapy or to chemotherapeutic agents.

The increased frequency of upper gastrointestinal hemorrhage, particularly from a bleeding peptic ulcer, may be related to increased acid secretion stimulated by hyperhistaminemia, and also by vascular mucosal ischemia caused by increased blood viscosity and poor regional perfusion.

Polycythemia vera usually evolves from an initial proliferative phase, during which therapy is aimed at reducing peripheral blood counts, to a stable phase, in which relatively normal counts may be maintained without therapy.[7] Eventually, the patient reaches a so-called burned-out or spent phase, due to progressive myelofibrosis and possibly to a reduced proliferative capacity of the abnormal hematopoietic clone.

In the past, the high incidence of fatal thrombotic or hemorrhagic complications in polycythemia vera reduced median survival to six to 18 months from the time of diagnosis.[5] Current treatment programs, which aim to maintain peripheral blood counts and red cell mass close to normal levels, have achieved median survivals of approximately ten years.

Early treatment with phlebotomy is intended to reduce the hematocrit to approximately 45%, in order to minimize the complications of hypervolemia and hyperviscosity. Patients over the age of 40 with polycythemia vera should receive some form of myelosuppression when the disease is complicated by the following: a platelet count greater than 700,000/μL; symptomatic splenomegaly; pruritus or gout not controlled by medical management; markedly increased red cell production requiring frequent phlebotomies; or medical contraindications to phlebotomy. This patient presented none of these features.

Initial treatment involves phlebotomy every other day or every third day, depending on the patient's tolerance of the procedure. Later phlebotomies are spaced further apart; when the hematocrit falls to 50–60%, weekly phlebotomies may be sufficient. The patient should be well hydrated in order to prevent relative hypovolemia, especially in view of the total liquid loss which phlebotomy involves.

Some hematologists prescribe oral iron to prevent progressive depletion of marrow iron stores with repeated blood removal. This patient showed such depletion, despite her faithful ingestion of multivitamins with iron.

This patient will be discharged from the hospital after anticoagulation therapy has been changed from heparin to coumadin. She will have weekly phlebotomies until her hematocrit is down to 40–45%.

Her initial PT and PTT, which were reported on admission to be markedly elevated, complicated the initial approach to heparin therapy; but elimination of the technical artifact, as Dr Urban described, convinced us that the patient most likely did not have an additional underlying coagulopathy. So the patient received a standard heparin dosage, which is most often effective—initially 2,500 to 3,000 units as a bolus, followed by 800 units per hour. We watched her closely for any bleeding. When her hematocrit is reduced to normal levels, we should no longer have this technical problem.

Jamshid Javid, MD (Director of Hematology, NYI-BDH; Director of Medicine, Goldwater Memorial Hospital): The first issue to be considered is that of diagnosis. With the clinical and laboratory data as presented, the diagnosis of polycythemia vera in this patient seemed very likely, but was by no means unequivocal. As emphasized by the Polycythemia Vera Study Group, the first requirement for diagnosis is to establish that the total volume of all red cells is increased, not just the hematocrit alone.

In a study of 100 consecutive patients suspected of having polycythemia vera,[4] some individuals with a hematocrit as high as 60% had contracted plasma volumes, with no increase in total red cell volume (so-called "spurious polycythemia"). In that study, all the patients with hematocrits greater than 65% had increased total red cell volumes; but this is not always the case. Since the diagnosis of polycythemia vera carries significant therapeutic implications, it would therefore be prudent to measure the total red cell volume directly in all patients in whom that disease is suspected.

Assuming that this patient does have a high total red cell volume, the next step in diagnosis would be to distinguish secondary polycythemia from polycythemia vera. This can be done in most cases by adhering to the criteria proposed by the Polycythemia Vera Study Group.[4] It should be noted, however, that these very stringent criteria were designed to exclude doubtful cases from the study; consequently, some patients with polycythemia vera may not fulfill these diagnostic requirements.

Assuming an increased total red cell volume, and given normal arterial oxygen saturation, the patient we are discussing satisfied two of the three major criteria, but lacked the third—that is, splenomegaly. In her case, the granulocytosis and the high neutrophil alkaline phosphatase level seemed to provide additional minor criteria in support of the diagnosis of polycythemia vera. But she had thrombophlebitis and so might reasonably be expected to have a high white cell count and an increased neutrophil alkaline phosphatase level as responses to inflammation. Unless these laboratory findings persisted after the inflammation subsided, their initial levels could not be used in support of the diagnosis of polycythemia vera. Such ca-

veats are clearly stated in the Polycythemia Vera Study Group criteria.

This patient underwent a bone marrow aspiration and biopsy which showed hyperplasia of all cellular elements. I do not consider these tests necessary or always helpful in establishing the diagnosis of polycythemia vera. Although patients with that disease, as a group, have characteristic marrow findings, an individual patient may not. More definitive tests must be done. Such biopsy studies, however, may be useful in assessing the degree of marrow fibrosis.

In cases in which a strong clinical impression of polycythemia vera cannot be confirmed by standard tests, one may resort to more definitive tests that help to differentiate secondary from primary polycythemia. These include the measurement of the plasma erythropoietin level, and the demonstration of erythropoietin sensitivity of erythroid progenitors in the bone marrow.

Patients with polycythemia vera have low levels of plasma erythropoietin, whereas those with secondary polycythemia produce excessive amounts of erythropoietin, either inappropriately or as a physiologic response to hypoxemia. However, even these straightforward relationships can be altered to some extent in patients with hypoxemia in whom a high hematocrit may have blunted the stimulus to increased erythropoietin production. In such patients, serum levels of erythropoietin in the upper ranges of normal may be found.[1] The true state of affairs can be unmasked, however, if the hematocrit is reduced to the 50% range by phlebotomy. When treated in this way, patients with polycythemia vera will continue to have low plasma erythropoietin concentrations, whereas patients with hypoxemia will respond with a clear rise in serum levels of erythropoietin.

When cultured in vitro, the primitive erythroid progenitors (burst-forming units, erythroid; and the colony-forming units, erythroid), obtained from patients with polycythemia vera can proliferate in the presence of erythropoietin concentrations that are too low to sustain the growth of normal erythroid progenitors.[8] This unusual sensitivity to erythropoietin, not shared by cells from patients with secondary polycythemia, can be used as a differential diagnostic test; however, the technical complexity of the cell culture process does not lend itself to routine clinical use.

The second issue I would like to address is the pathogenesis of polycythemia vera.[2] Studies using X-chromosome markers[6] have shown that, at least by the time the disease is diagnosed, in each patient all hematopoietic cells (erythrocytes, granulocytes, and platelets) represent the progeny of a single pluripotential hematopoietic stem cell. Taken together, these features suggest a model, although oversimplified, which indicates that the initial event in the development of polycythemia vera may be a mutation in a single multipotential hematopoietic stem cell. The progeny of this cell have heightened sensitivity to the appropriate growth factors. In the presence of normal concentrations of these growth factors, the clone of mutant cells has a growth advantage over their normal counterparts, leading to a gradual increase in the mass of the mutant clone and feedback inhibition of the production of the growth factors to a low level. This level will still support the proliferation of the sensitive clone, but not of the normal cells.

In polycythemia vera, most of the major clinical features can be traced, directly or indirectly, to the increased red cell mass, including the thrombotic episodes that are a predominant cause of morbidity in this disease.

What role, then, does the increase in platelets play in the pathogenesis of polycythemia vera and its complications? Surprisingly, the thrombotic episodes do not correlate well with the incidence of major thrombocytosis.[9] However, in the study cited, the higher the hematocrit, the greater the number of thrombotic episodes per patient-year. For patients with hematocrits greater than 60%, the rate of thrombotic episodes was more than ten-fold higher than in those patients with hematocrit values between 40% and 44%. Similar findings have been reported by other groups.[5] An aspect that has not been fully explored is whether an increase in platelets further increases the risk of thrombosis in patients with high hematocrits.

The efficacy of agents that inhibit platelet aggregation is under study by the Polycythemia Vera Study Group. As quoted by Berk et al,[5] the antiplatelet agents, in the dosages used, did not affect the incidence of thrombosis but did increase the rate of bleeding, as compared with a placebo. In any case, the maintenance of a normal hematocrit is now a major end-point in the management of this condition.

I agree with Dr Urban's explanation of the artifactual prolongation of the prothrombin time and partial thromboplastin time in this patient. This problem can also be avoided if part of the anticoagulant is removed from the tube before the addition of the blood sample, in order to compensate for the small plasma content of polycythemic blood. With a hematocrit of about 50% or lower, this precaution is not necessary. It should be noted, however, that a significant fraction of patients with polycythemia vera have real abnormalities in their clotting factors. A significant incidence of deficiency of Factor V[10] or of Factor XII[11] has been described. The mechanisms of these deficiencies are not clear, but low-grade disseminated intravascular coagulation may play a part. These findings do not seem to correlate with either the bleeding or the major thrombotic complications that attend the course of polycythemia vera.

The management of patients with polycythemia vera has been evaluated by the Polycythemia Vera Study Group. The patients under study were divided into three groups: one treated with phlebotomy alone; a second treated with phlebotomy plus chlorambucil; and the third treated with phlebotomy plus radioactive phosphorus. The long-term course and survival of these groups have indicated the following[5]:

1. In the first four or five years of treatment, the three groups had similar mortality rates. There was, however, a significant increase in the rate of nonfatal thrombotic episodes in the patients who were treated with phlebotomy alone.
2. Over the next ten years or so, the mortality in the other two groups exceeded that in the group treated with phlebotomy alone. This increased mortality was primarily due to a higher incidence of neoplasms, including acute leukemia, various carcinomas, and lymphoblastic lymphomas.

Currently, treatment with hydroxyurea as an adjunct to phlebotomy is under study.[12] This agent is thought to have a low leukemogenic potential. It is effective in controlling cell counts in polycythemia vera, but its effects are short-lived, so that long-term continuous therapy may be necessary.

Patients with polycythemia vera who have very high platelet counts over a long period of time seem to have a higher incidence of marrow fibrosis. This may be related to the fact that platelets and their precursors in the marrow, the megakaryocytes, produce a protein (platelet-derived growth factor) which structurally and functionally is very similar to the product of simian sarcoma virus oncogene.[13] This material can increase the proliferation of fibroblasts in tissue culture. The presence of a great many megakaryocytes in the bone marrow may lead to a local increase in the concentration of platelet-derived growth factor, with consequent fibrosis. Perhaps from this point of view alone, it may be useful to try to reduce the megakaryocyte and platelet count. From the standpoint of prevention of thromboses, however, patients with platelet counts of up to one million need not be treated, as alluded to before.

In summary, phlebotomy is to be included in the management plan of all patients with polycythemia vera. On the basis of long-term studies,[5] the Polycythemia Vera Study Group recommends that additional treatment with radioactive phosphorus be given to patients older than 70 years, in view of their greater chance of suffering thrombotic episodes. For younger patients, especially those under age 50, treatment with hydroxyurea should be given only in the presence of additional risk factors for thrombosis, or if the need for phlebotomy proves excessive.

Satish Dhalla, MD (Attending Physician): In primary thrombocytosis, where there is a relatively normal hematocrit, there is a tendency to thromboses. Are there other qualitative differences between those platelets and the ones which we see in polycythemia vera?

Dr Javid: I am bothered by the same question, and I do not know the answer. Perhaps the thrombotic tendency is, in part, due to the higher platelet counts found in patients with primary thrombocytosis.

John T. Flynn, MD (Associate Chief of Medicine): We are blaming this patient's headaches and blurred vision on the polycythemia. But since you have questioned to some extent the diagnosis of polycythemia vera, do you feel that a CT scan of the brain is indicated?

Dr Javid: I am not really questioning the diagnosis of polycythemia vera, merely the completeness of the evidence for it. You are suggesting that we might want to rule out a cerebellar hemangioblastoma or a tumor of the floor of the fourth ventricle, which have been known to lead to a secondary polycythemia. I feel that this patient does in fact have polycythemia rubra vera, but I wanted to emphasize some of the problems and uncertainties that we face in making that diagnosis.

Dr Flynn: Could this condition be controlled by deliberately producing an iron deficiency anemia with repeated phlebotomy?

Dr Javid: Patients with polycythemia vera usually have reduced marrow iron stores and may have microcytosis even before phlebotomy. It is reasoned that their iron stores are reduced because the iron is tied up in their increased mass of hemoglobin. Possibly, however, they have iron stores in areas other than the marrow, as evidenced by the observation that they can quickly replenish their hematocrits after repeated phlebotomy. Eventually, after the removal of considerable amounts of blood, they do become iron deficient and require less frequent phlebotomy.

Administering iron to correct the deficiency will make control of the hematocrit by phlebotomy more difficult. An interesting aspect of this question, reported several years ago,[14] is that at any given hematocrit value, a lower mean corpuscular volume of the red cells is associated with a higher viscosity, and, presumably, a greater risk of thromboses. So there may be conflicting interests as to whether to allow iron deficiency to develop in these patients.

Dr Urban: Could erythropoietin be given to patients with polycythemia vera, in order to stimulate the normal marrow precursors and perhaps crowd out the abnormal clone?

Dr Javid: That has not been done, to my knowledge. At least in the early and middle stages of the disease, normal red cell progenitors are present in the bone marrow and can be made to grow in tissue culture. Whether the induction of their growth in vivo would have a salutary effect on the course of the disease, I do not think is known. It may be impractical to try this, because it would make control of the hematocrit more difficult, and it would require large amounts of erythropoietin to be administered over a prolonged period of time.

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A historical overview of the recognition of appendicitis—Part I*

DALE C. SMITH, PHD

One hundred years ago, on June 18, 1886, Reginald Heber Fitz[1] read his classic paper, "Perforating Inflammation of the Vermiform Appendix; with Special Reference to its Early Diagnosis and Treatment," before the first meeting of the Association of American Physicians in Washington, DC. The received wisdom is that "It made a profound impression not only on his immediate audience on that eventful day in Washington, but on the entire medical profession."[2] Since very early in this century Fitz has been given credit for effecting a revolution in surgery. At Fitz's memorial service on November 17, 1913, W. W. Keen[3] said, "Fitz struck a note that we all heard and heeded... As a result of these papers the profession quickly recognized the deadly role of the appendix in inflammations in the right iliac region, and from then until now hundreds and even thousands of operations have followed each other..." Many others have agreed with Keen.[4-7] This paper, too, celebrates Fitz's work and contribution to the medical profession's understanding of appendicitis, but it attempts to present a more balanced and historically accurate story. There was no revolution (there seldom is in subjects as complex as health and disease), but there was a steady evolution, both of scientific knowledge and of the profession's ability to aid the patient. In that evolution Fitz played an important role but, as important as his role as pathologist was, equally important was his recognition that he lived in an era of change, when surgery was making great strides and when issues were being raised that remain in the center of medical debate.[8]

At the beginning of the 19th century the medical profession had lost the confidence of the public and was widely considered to be ineffective. Modern scientific medicine emerged in a recognizable form in the 19th century, and by the 20th century had achieved wide public acclaim. Many elements were involved in this change of attitude—a general appreciation of science, the great improvement in public health by means of sanitary reform, and, perhaps more than anything else, the emergence of effective modern surgical intervention techniques.[9] Because surgery had relatively little impact on the major causes of mortality in western populations it is often overlooked by social historians attempting to explain the triumphant transformation of medicine in the 19th century. However, successful surgery had profound social effects, as it provided dramatic interventions that relieved pain and prolonged life in numerous cases. One only has to consider the case of the rural Minnesota mother who, late in the 19th century, was seen putting her child on the train to Rochester unaccompanied by an adult. When asked what she was doing she showed bystanders a card pinned to the child marked, "The Doctors Mayo, Rochester," and explained that the doctors would make her child well again.[10] Or consider the case of the friend, family member, or neighbor whose life was dramatically changed by the surgical removal of a large goiter. Or, as a final example, consider the case of the person who fell ill with severe abdominal pain which the local physician diagnosed as "inflammation of the bowel." Everyone knew people who had died in pain from that condition. Now, however, the surgeon was able to intervene, diagnose appendicitis, and perform an appendectomy. The patient recovered completely and lived a long and happy life. These are the socially small, population-insignificant events, happening on an individual level, which in the aggregate make up a social transformation, and which made a major contribution to the triumph of modern medicine.

Numerous factors made possible such successful interventions. By looking at the historical record of one condition, it is possible to observe many of the variables as they came together to create the change. Appendicitis is a particularly good example, since it was one of the major abdominal procedures that helped convince both the medical profession and the public of the change that had occurred. But in order to fully understand the change, it is necessary to go back prior to the success and look at the level of knowledge available and the effect it had on patient care. American medicine in the mid-19th century was not monolithic. The best physicians of the east coast were as good as those anywhere. Many practitioners were good—both on the east coast and in the interior valley—some were terrible, and some were quacks.[11]

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Pathological Lesions of the Appendix

By 1855 pathological anatomy had been established as the science on which medical progress was founded. The great French physicians of the early 19th century had pioneered the study of disease by establishing the correlation between clinical signs and symptoms and the lesions observed postmortem. A generation of American physicians had traveled to France to study under the leaders of Paris medicine—Laennec, Andral, Velpeau, Nelaton, and Dupuytren—and above all to study with Pierre Louis and to learn the use of the numerical method in clinical research. American physicians had returned to teach the same methods, methods which Austin Flint and Frank Hamilton brought to Buffalo and in which Dr Thomas F. Rochester was well versed.

Dr Rochester, assistant to Dr Flint at the Hospital of the Sisters of Charity and the Buffalo Medical College, was typical of America's good physicians, and perhaps a little better than most.[12] At the November 1855 meeting of the Buffalo Medical Association, Dr Rochester presented a pathological specimen. He reminded the assembled physicians that this was the third such specimen he had presented to the group—all three postmortem specimens of perforation of the intestine at the appendix vermiformis.

On October 19, 1855, a coachman, James Rose, had suddenly been taken ill with what he supposed to be an attack of "gravel." In the finest American tradition of self-reliance, Mr Rose, having made his own diagnosis, dosed himself with oil, and on the next day was well enough to return to his work. In the afternoon he had a sharp chill with pain and dysuria but, secure in his opinion that the cathartic would bring relief, he took more oil and went to bed. On October 21, Dr Rochester was summoned, and found the patient suffering spasmodic pain and producing scanty urine stained with blood. On insertion of a catheter the bladder was found to be empty. Nausea, some vomiting, and great abdominal tenderness were present—in fact, all the symptoms of severe peritonitis. Dr Rochester felt that the most probable cause was a renal calculus that had perforated the ureter, resulting in peritonitis from urinary infiltration. He prescribed morphine as needed to relieve the pain and antiphlegmatic measures to combat the inflammation. The patient declined steadily and died on October 23. Dr Rochester reported the postmortem findings to the medical association:

> The kidneys, ureters and bladder were healthy. The peritoneum exhibited a grade of peritonitis more severe and extensive than either [he or Dr Flint] had ever met before. Large patches of gangrenous peritoneum were scattered over the visceral surfaces, some of them several inches square, but the center of inflammatory action was evidently about the caput coli. The smell being extremely offensive, the abdominal contents were removed to the dissection room of the college for examination. The appendix vermiformis was found firmly glued down to the caput coli, so much so that it required the knife to release its distal extremity. On turning it up, the perforation was found at the inferior surface of the junction of the appendix to the colon. *Within* the appendix was found a bean, which was the evident cause of death.[13]

FIGURE 1. Thomas Rochester, MD (1823–1887). Buffalo physician, typical of early American practitioners interested in disease of the appendix.

Within two years Dr Rochester, then a professor in his own right, having succeeded Flint at both the college and the hospital, reported another similar case. This time the patient was a child who had had a severe abdominal attack three days before. On the basis of the severe abdominal pain and generalized tenderness Rochester could only diagnose peritonitis. At the postmortem examination three days later peritonitis was confirmed; fecal matter was found in the lower portions of the abdominal cavity. The appendix was gangrenous, adherent to the rectum, and contained a bean-sized fecalith. At the discussion before the medical association Dr Rochester advanced the opinion that such perforations of the intestine at the appendix were a much more common cause of peritonitis than had been generally realized. In a study of the literature he found that only one author, the great Viennese pathologist Karl Rokitansky, indicated that such disease was not an infrequent state.[14]

Thomas Rochester's knowledge of pathological anatomy was excellent; his knowledge of the medical literature, however, was poor at best. Books and journals of the period contained numerous references to perforation of the appendix and inflammations resulting in peritonitis. The study of peritonitis and disease of the appendix had its origins in Europe, and pathological observations both surgical and anatomical had been made in the 18th century. In the first third of the 19th century the new approach of clinical pathological correlation had been applied to peritonitis originating in the right iliac fossa. The observations of disease of the appendix made in Paris by J. B. Louyer-Villermay[15] and F. Melier[16] and in England by Richard

FIGURE 2. A necropsy specimen of pathology of the appendix. The case record does not survive but the specimen was one of those donated to the College of Physicians of Philadelphia by Thomas D. Mütter (1811–1859). Photograph courtesy of the Mütter Museum, The College of Physicians of Philadelphia.

Bright and Thomas Addison[17] were never lost sight of by pathologists, but they had no clinical reality. Guillaume Dupuytren, the great French surgeon of the early 19th century, preferred to use the terms perityphlitis, disease of the tissue around the cecum, and typhlitis, disease of the cecum, since clinically those were believed to be the important divisions. Disease of the cecum, frequently the result of blockage, could be treated by evacuation, while inflammation of the adjacent tissue suggested antiphogistic remedies and opiates.[18]

As Americans studied in France and brought home the idea of clinical pathological correlation, they formed societies and associations to discuss their medical research. One typical group was the Philadelphia Pathological Society where in 1838 Edward Hallowell, Jr,[19] initiated discussion of perforation of the appendix and peritonitis. This began a tradition which led William Pepper, Sr,[20] who had also studied in Paris and contributed to the study of peritonitis by postmortem analysis, to comment in 1845: "Such cases can no longer be considered as extremely rare, since numerous instances of a somewhat similar character are now to be found on record."

In 1851, E. Hartshorne[21] added the 44th specimen of a ruptured appendix to the pathological cabinet of the College of Physicians of Philadelphia. Similar events took place in the meetings of the New York Pathological Society and the Boston Society for Medical Observation.

By 1855, when Rochester presented the case of the coachman Rose, this growing literature was having an impact on the best of American physicians. The case of F. M. Robertson, a physician and medical teacher of Charleston, South Carolina, illustrates a common point. In 1855 Dr Robertson[22] published a straightforward paper in which he described rupture of the appendix, commenting that it was the third such case he had studied. The first case, occurring in 1847, had been reported as cecal abscess despite the fact that the appendix was filled with a "substance resembling old cheese" and the tissue coats of the organ were "entirely destroyed by ulceration at one point." There were also two ulcerations opening the cecum so the more general diagnosis seemed in order.[23] By 1855 the combined effect of the literature and the fact that his third case, while clinically similar, was without cecal openings led to Robertson's greater pathological and nosological precision.

In 1857, the year Thomas Rochester of Buffalo was citing Rokitansky, Caspar Wister gave a review of disease of the appendix before the College of Physicians of Philadelphia. He discussed the anatomy of the organ, presented two cases of his own, and reviewed the international literature. He noted that the "disease [was] deficient in symptoms sufficiently distinct for satisfactory diagnosis; and only decided in the steadiness with which it resisted treatment." Dr Wister believed that the disease—ulceration of the appendix—was not necessarily fatal, but that successful intervention would require diagnostic good luck and great anatomical knowledge. The disease resulted in abscesses which pointed in various directions according, Wister believed, "to the variety of directions assumed by the appendix; and it is of great moment that these should be anticipated and discharged at the earliest period possible and the risk of an internal rupture of their walls diminished." James Levick, in discussion of the paper, remarked that "it would be a matter of interest to ascertain if there were any particular symptoms which would enable us to localize during life the seat of diseases of this kind."[24] A similar review had been prepared by George Lewis[25] of New York City the year before.

In 1867 Rochester again brought the disease to the attention of the Buffalo Association, reporting a case seen in consultation with a clinical history strikingly similar to that of the coachman Rose whose case Rochester had reported in 1855. The original diagnosis was right ureteral colic, but when Rochester saw the patient he diagnosed "a localized peritonitis with disease of the vermiform appendix." At autopsy a perforated appendix was found. Rochester's comments in 1867 suggested an extensive knowledge of the disease; he pointed out its difficulty of diagnosis, noting particularly its similarity to renal colic; he commented on its greater frequency among young adults; and noted that the foreign bodies, often found at autopsy and variously described, were "usually concretions of hard fecal matter." He noted that the condition was not invariably fatal—the peritonitis could be localized in an abcess which could burst into the intestine or through the abdominal wall and from which the patient

might recover. He had seen one patient with each of these favorable terminations.

The greatest change in the discussion of 1867 was not the greater pathological knowledge available to Dr Rochester after 12 years—Karl Rokitansky had known as much 20 years before —but rather the comment that Dr Willard Parker of New York City had intervened surgically for the condition and had successfully drained the abscess. The 1867 Buffalo case would have, in Dr Rochester's opinion, lent itself to Parker's operation—the disease was confined to the appendix which "could have been removed entirely but this could not be foreseen or conjectured even and the event might have been just as fatal." Dr Rochester's belief in 1867 was that "the possibilities of spontaneous favorable issue are greater than the probability of successful surgical operation."[26]

Rochester's experiences on the fringes of medical progress in Buffalo, New York, were hardly unique. Numerous scholarly physicians recognized the disease of the appendix and variously estimated its frequency. For a generation Rokitansky was the leader of the science of anatomic pathology and personally taught vast numbers of students; he reached even more through his great pathology text. But even after Willard Parker had done it successfully, the cure, surgical intervention, was considered by most physicians to be even more dangerous than the disease itself. The reason for this attitude is well known: the year Parker published his results, 1867, was the great dividing line in surgery—the year Joseph Lister published his first paper on the antiseptic treatment of compound fractures and so began a revolution in surgery.

Surgical Intervention—The Willard Parker Operation

What then prompted Willard Parker to intervene in a pre-Listerian age when the abdomen was considered inviolate by most surgeons? Was he simply reckless but lucky? Probably not; like all successful surgeons, Parker could be bold when necessary, but he was a thoughtful and carefully trained surgeon. He had studied with the great John C. Warren at the Harvard Medical School in the days before anesthesia. He had had the benefits of postgraduate training in France under the leaders of Paris surgery and for over 20 years had been a professor of surgery and a surgical consultant in a variety of places in the United States. With the introduction of anesthesia, greater possibilities for surgical intervention were opened, and Parker was one of America's leaders in operative progress in the mid-19th century. In 1867 he was Professor of Surgery at the College of Physicians and Surgeons in New York. Parker knew more of the surgical and pathological literature than did Thomas Rochester in Buffalo, so he knew that anatomic pathologists, following the lead of Dupuytren, had described at least two conditions of the right side of the abdomen: typhlitis and perityphlitis. Parker knew that in cases of perityphlitis, which were frequently associated with disease of the appendix, patients had a localized peritonitis, walled in by the body. Sometimes this abscess pointed to the surface or ruptured into the intestines; most of the time the wall broke down and general peritonitis resulted. Since 1843 he had drained those abscesses that pointed externally, recognizing that he was only assisting a natural process. Willard Parker, like many of America's best practitioners of the mid-19th century, had learned to trust nature. Beyond unassisted recoveries Parker pursued the problem with the question, "Are the efforts of nature exerted internally in such a case, and if so, in what way?" Parker believed nature attempted to localize the abscess and then discharge the accumulated pus. The surgeon could intervene after the wall had formed localizing the abscess, and regulate the discharge of pus to the exterior. It would be important to intervene before the wall broke down but after it was fully formed. Parker[27] believed that was between the fifth and the 12th days.

Despite his knowledge of the condition, his trust in the healing power of nature, and his belief that he understood the appropriate way for the surgeon to intervene, Parker did not dare the operation until tragedy made him desperate. His son-in-law later recalled that Dr Parker told him of having attended the "autopsy of a young girl, the daughter of an old and valued friend," and of having resolved that he would interfere surgically if the chance presented itself in the future.[28] When Parker next encountered a case of circumscribed tenderness in the right abdomen which he thought to be perityphlitis he acted. No evident swelling or fluctuation was yet present, but Parker incised the skin, felt a tumor-like localized abscess, and drained it. The wound healed by granulating and the patient completely recovered.

Parker's experience was hardly unique; Wister had seen the need for surgical intervention ten years before Parker published his report, and in 1848 Henry Hancock[29] of London had done a similar operation and reported it prominently and completely. There were other British attempts following Hancock's experiences.[30] Surgeons had long engaged in draining abscesses and even abscesses of the abdomen had been considered subject to the lancet by leading surgical teachers of the 19th century such as Dupuytren of Paris,[18] Syme of Edinburgh,[31] or Gross of Philadelphia.[32] However, abscesses were only drained when fluctuation was evident, when they were ripe. Parker intervened in 1843 and then waited over 20 years before he intervened again, at least according to his published cases. Part of the problem for Parker as for Wister and others was diagnostic:

> Familiar as we are with the diseases to which the alimentary canal is liable there is one part of it—the appendix vermiformis—the pathology of which is, to a great extent, involved in obscurity . . . and this neglect is not to be wondered at, when we reflect that by its position, the appendix vermiformis is insignificant; and by its anatomical similitude with the rest of the intestinal tube it is impossible for disease affecting it to remain for more than a limited period, local . . . frequently it is only at the autopsy that we become acquainted with the precise nature of the disease which has terminated the life of the patient.[27]

Parker felt there were three distinct disorders frequently grouped together under the name of typhlitis: gangrene of the appendix, perforation of the appendix, and abscess of the appendix. He acknowledged that there might be, as some pathologists thought, a catarrhal appendix precursor to all three, but clinically and at postmortem examination the condition was unidentifiable. Parker acknowledged that for gangrene or perforation neither medicine

FIGURE 3. Henry Hancock (1809–1880). London surgeon, best known for his development of the Hancock operation for ankle amputation. He performed an incision-and-drainage operation for appendicitis-induced local peritonitis in 1848.

nor surgery could offer the patient hope. For abscess, though, he could, as a bold surgeon, assist nature to heal the patient. Parker was describing a particular pathological phenomena; he did not identify the abscess of the appendix as perityphlitis. Perityphlitis was a clinical entity which had several possible seats, one of which was the appendix. An extensive, independent pathological literature existed on disease of the appendix, but pathological distinctions without clinical reality were largely ignored by most practitioners.

In 1866 Roberts Bartholow,[33] an influential medical teacher and researcher in Cincinnati, published an extensive review of perityphlitis in the *American Journal of the Medical Sciences*. If there was a journal in 19th century America that enjoyed wide readership and high prestige, it was the *American Journal*; its only close rival would have been the *Boston Medical and Surgical Journal*. In his paper Bartholow examined the "disease, either of the caecum, appendix, or peri-caecal tissues which ends in the formation of an abscess in the right iliac region." The abscess was the condition of clinical interest and Bartholow felt that efforts to identify its origins had been confused. Bartholow was convinced that the older view, dating back to Dupuytren, that "an idiopathic inflammation occurred in the sub-caecal tissue," was wrong. Pathological research had established that such inflammations were "a very secondary part in the phenomena of abscess of the right iliac fossa." However, the narrow view (identified with John Burne[34] of the Westminster Hospital in London and with writers working in east coast urban hospitals) that all abscesses were "tuphlo-enteritis" or exclusively the result of "ulceration and perforation of the appendix" was too limiting. (Tuphlo-enteritis was John Burne's term, introduced into Boston by J. B. S. Jackson. It was used consistently by Boston pathologists from the early 1840s through the 1870s.) Abscesses that resulted from caecitis were "a form of disease not infrequently met with in the interior portion of this continent." Bartholow noted that these abscesses spread and caused general peritonitis. In general he believed that the practice of Dupuytren was proper and sufficient—bleeding, fomentations, poultices, baths, lavements, and laxative drinks were endorsed as supportive—but that the healing power of nature was best. "In my experience nature is very competent to manage the case." The prognosis was dependent on formation of the localized abscess: "a final result may be anticipated, do what we will, unless adhesions localize the inflammation." If an abscess formed, "in a majority of cases recovery ensues." Bartholow was aware of the surgical approach to the management of these abscesses. He cited the recommendations of Gurdon Buck, a New York surgeon, who had classed right iliac abscesses with other deep-seated abscesses and who from at least 1861 had recommend-

FIGURE 4. Willard Parker, MD (1800–1884). Professor of Surgery, College of Physicians and Surgeons, New York, who popularized the incision-and-drainage operation for perityphlitis in 1867.

ed surgical drainage. Bartholow[33] wrote, "I think it not well to make haste to use the knife," in part because "bursting of the abscess into the peritoneum is an accident not to be apprehended in these cases."

Not every practitioner agreed with Bartholow concerning the use of the knife, particularly once fluctuation was detected. A. T. Hudson of Lyons, Iowa, wrote of a 37-year-old engineer who recovered following surgical drainage of a typhlitis. Hudson probably expressed the professional opinion of most practitioners at the time Parker was publishing that, "whether this was an abscess of the vermiform appendix, the caecum, or both, is a question which cannot be clearly determined. . . . Probably, in every severe case, both are involved." Pathological precision was clinically difficult—"the difficulty of diagnosis at an early or progressive stage of the disease, is mentioned by eminent observers as very puzzling . . . "—and practically of little importance—"recovery or a *post mortem* reveals the truth."[35]

What is the significance of Willard Parker's 1867 paper? Simply that for 20 years the Parker operation or incision dominated the treatment of right iliac abscess; from the date of Parker's paper there was therapeutically no looking back. Early in 1875 when Thomas Rochester in Buffalo was asked by Michael Hayes to treat an abscess that "had recently appeared in the right iliac region," Rochester diagnosed perityphlitis and called "Dr. J. F. Miner to see him in consultation and to go prepared to operate."[36] Three contributing factors explain the change in treatment methods and coincidentally Willard Parker's success as an advocate of surgical therapy. First and foremost is the social and scientific progress in surgery, second is the example of success in gynecologic surgery, and third is a continuous tradition of advocates who taught each other, passing on the torch, until by 1889 Charles McBurney developed a surgical approach that was recognizably modern.

We do not frequently think about surgical progress in the mid-19th century because it has been so dramatically overshadowed by the achievements of the last century's end and those through the 20th century. The great progress of antiseptic and aseptic surgery is, of course, part of the story of appendicitis. The surgery became steadily safer over time, but there was an earlier generation that was post-anesthesia and pre-antisepsis. In addition to the general progress in the knowledge of anatomy, Americans experienced the added spur of the practical necessity for improved trauma surgery during the Civil War. With the availability of both anesthesia and wider experience, surgical therapy was more acceptable to both the public and the profession in the late 1860s.[37]

The change in surgical acceptability may, in part, explain the long lapse in cases reported by Parker. His first patient, Dr T., was treated in 1843 and was still living in Brooklyn in December 1866.[27] This physician could have been either John Sullivan Thorne or Joseph Turner (the only two practitioners with surnames beginning with "T" in practice in Brooklyn in 1843 and 1866)—both would have been known to Parker's audience. That a physician was the first patient may be explained by the fact that a physician may have better understood the risks and benefits of Parker's approach and so may have been willing to submit to a surgical therapy when a layman might not. The next case Parker reported was from mid-1865, that of a Mr D., who was stricken May 20 and operated on June 17. In 1865 Parker would have been aware of Gurdon Buck's campaign to treat deep abscesses surgically. He and Buck were both members of the New York Pathological Society where Buck first advanced the idea, and they were fellow members of the surgical staff of the New York Hospital.

Dr Buck's experience was principally with deep abscesses of the neck, but he reported one case of abscess in the iliac fossa before the New York Pathological Society on April 26, 1865. There was a palpable swelling, which Dr Buck opened over its posterior portion. He reported:

> I cut down carefully, and satisfied myself I could transmit an impulse from the portion of the swelling occupying the fossa anteriorly to this posterior portion which was resonant. The question was whether the gut had not made its way to the surface, but the transmission of the fluctuations from one portion of the swelling to the other settled the question that such was not the case.[38]

Parker was a better trained anatomist and clearly a better informed physician concerning the pathological literature. His approach was more direct, earlier, and more rational than Buck's; but Buck's efforts may have contributed to his willingness to once again attempt surgical therapy in a case of right iliac abscess.

The Dissemination of Parker's Operation

Parker published his work in a new journal, the *Medical Record*, which, as a weekly medical journal, ushered in a new standard for medical periodicals in the late 19th century. Its editor, George F. Shrady, maintained the highest standards and met the needs of practitioners for practical information on a regular basis. The latter third of the 19th century saw important progress in the medical literature, including the introduction of the *Annals of the Anatomical and Surgical Society* of Brooklyn, which in 1885 became the *Annals of Surgery*, the first periodical in English devoted exclusively to surgery. Another means of exchanging information also developed in the last quarter of the century—the surgical society. On a national scale, the American Surgical Association, and on the local level, the New York Surgical Society, as well as the Anatomical and Surgical Club of Brooklyn and the Philadelphia Academy of Surgery all provided surgeons with forums in which to discuss surgical therapy.[39-42]

The second factor that contributed to the progress of surgical therapy for appendicitis was the development of the field of gynecology, particularly surgical gynecology. The contributions of James Marion Sims (1813–1883) are well known but it is frequently forgotten that while he began his work on the surgical repair of vesicovaginal fistulas in Alabama, he moved to New York in 1853 and continued his pioneering work from the Women's Hospital. Sims' introduction of gynecologic surgery in New York City was impressive; he repaired a complete laceration of the pelvic floor in a patient referred to him by Gurdon Buck after Buck had failed twice. During the 1860s Sims pioneered new techniques of ovariotomy and trained other surgeons to perform his new operations. At Women's Hospital he was followed by Thomas Emmet, Ed-

mund R. Peaslee, and Theodore G. Thomas.[43] In 1872 Robert Battey introduced the idea of oophorectomy for nonovarian conditions. Within a relatively short time conservative surgeons were complaining about what they perceived to be a rash of unnecessary laparotomies.[44] To cite two limiting examples from the New York City medical literature, in 1857 (the year of Wister's review article) Edmund Peaslee[45] published a paper pointing to the diagnostic difficulties in isolating the anatomical seats and causes of abscess, in particular the differentiation between pelvic disease in women and perforation of the appendix. And one volume of the *Medical Record* ran a synopsis of Fitz's[46] paper presented at the Association of American Physicians meeting, a synopsis of a paper from the *Dublin Journal of the Medical Sciences* entitled "The So Called Laparotomy Epidemic,"[47] and a report of Thomas Emmet's[48] paper presented at the American Gynecological Society meeting in which he explained the differential diagnosis of pelvic cellulitis (PID?) and peritonitis.

The final contribution to Parker's success was the simple fact that he had followers. Henry Hancock was a well-known and influential surgeon in mid-Victorian London but he did not enjoy the equivalent of Parker's academic position. Since 1839 Parker had been Professor of Surgery at the College of Physicians and Surgeons of New York and was a surgeon at the New York Hospital. In 1867 he was the senior academic surgeon in the American city that trained more physicians than any other. He was New York's foremost surgical consultant and a consulting surgeon at most of the city's hospitals. In 1860, he took as his partner in practice Henry B. Sands, one of his former pupils, who had been moving steadily from a general family practice into surgery. In 1867, Parker arranged Sands' election to the faculty of the College of Physicians and Surgeons as Professor of Anatomy. In Parker's paper of 1867, Sands was named as his assistant in the operations of 1865–1866. When Parker resigned the chair in surgery at the College of Physicians and Surgeons in 1869, Sands did not have enough seniority to replace him, but he did become one of the joint occupants in 1879. Sands was the organizer of the New York Surgical Society and among his private pupils were William T. Bull, Reed B. Bontecou, and William S. Halsted, all of whom would contribute to the surgical treatment of perityphlitis. Of greater significance was Sands' association with Charles McBurney, whom he appointed as his demonstrator in anatomy in 1872 and his demonstrator in surgery in 1880. McBurney had been a student at the College of Physicians and Surgeons when Parker introduced the operation. When Sands died suddenly in 1888, McBurney became Professor of Surgery at the school, a post he held until 1907. McBurney's papers of the 1880s demonstrate and acknowledge his debts to Sands. Thus for 40 years following Parker's publication there was an influential advocate of surgical therapy in New York City who had been intimately involved with the development of that therapy.

It did not take long for Parker's 1867 paper (or at least his idea) to have an impact.* Just before Parker published his paper, J. Hobart Burge of Brooklyn was called to see a young lady with classic symptoms: after two weeks there developed "a firm mass in the right inguinal region which [was] tender on pressure." The next day, three days after

FIGURE 5. Henry B. Sands, MD (1830–1888). New York surgeon, the leading proponent of the Willard Parker operation in the late 1870s and 1880s.

Parker's paper appeared, Dr Burge called Parker into consultation and "at my request he operated." The patient made an uneventful recovery.[50] Burge was typical of 19th century urban practitioners who frequently get submerged in modern generalizations about professional competition and school rivalries. A graduate of the medical school of New York University, he taught as a surgeon on the wards of a rival medical school, The Long Island College Hospital. Yet when his patient experienced a crisis in which a local rival would be the best person to provide care, the rival was called in and given the priority—and, of course, the risk of holding the knife.

In 1871 Leonard Weber "read an extended paper" on abscess of the appendix to the meeting of the Medical Society of the County of New York. He explained that the abscess was "usually due to perforation of the appendix, from inflammation and ulceration dependent on a fecal concretion, or much more rarely a foreign body impacted within it. In the process of ulceration, local peritonitis may be set up, forming adhesions, and so separating the affected part from the general peritoneal cavity . . ." Dr Weber described cases of abscess he had seen, one of which he

* It seems likely that Parker had discussed or taught the new operation before the paper was published. In 1874 Samuel Whitall published a report of a case in which he used the Parker incision, and he reported that the procedure was "proposed by Dr Willard Parker in 1865."[49] Whitall was a student at the College of Physicians and Surgeons in 1865 and may have been recalling some verbal account. Of course it may also be an error.

had recently treated using the Willard Parker incision. He modified Parker's operation in that he cut down to the transversalis fascia and allowed the abscess to rupture the fascia, reducing, he felt, the risk of surgical infection.[51] Henry Sands was among the physicians who discussed Weber's paper and he described a case in which he had observed Parker operate but which Parker had not published a report of. "It was obscured by the absence of any circumscribed swelling, the feeling being that of deep-seated oedema of the parietes of the iliac fossa. . . ." Parker's experience and clinical judgment were seen by Sands as crucial and he recounted two cases seen by Parker where he did not operate and the patients recovered.[52]

In the same discussion Dr Ernst Krackowizer reported on three patients. One of these he had seen 13 years earlier; Dr Alfred Post had drained the patient's abscess which then recurred twice, and Dr Krackowizer drained it both those times (the patient then remained well). The second patient was a boy seen the previous August and September. In that case a "tumor, sharply defined and a little smaller than a hen's egg," was detected in the region of the pylorus, but no operation was attempted. The boy died. At postmortem Krackowizer observed old adhesions binding down the appendix. He speculated that they might give some insight into the pathogenesis of the problem or the confusing placement of the abscess. From such discussions it appears that Parker's operation was seen primarily as an intervention that took place earlier than was common, but not as a fundamental departure in therapy.

In February 1872, one of Sands' pupils, William Bull, presented an MD thesis on perityphlitis to the College of Physicians and Surgeons and was awarded the first prize for his year. The work is typical of the best of American medical theses of the 19th century, revealing the strengths and weaknesses of an evolving system of medical education. Dr Bull's thesis must reflect his own reading and Sands' teaching. He used the literature but did not read carefully, thus missing things Sands knew, but the broad outlines are the received wisdom of 1872. Bull discussed the Greek origins of the term perityphlitis, a term he felt was preferable to other names, including abscess of the iliac fossa, phlegmonous tumor of the iliac fossa, and abscess of the appendix vermiformis. "The last named of these is really inaccurate for it expresses a condition which does not exist . . ." By 1872 there was agreement that Parker's differentiation of gangrene, perforation, and abscess of the appendix was a misdirection. The abscess seemed to result from either perforation or ulceration of the appendix, but this was not the only cause. Bull noted:

> In most cases perityphlitis is secondary to disease of the caecum or appendix vermiformis. It occurs however, as an independent affection from the influence of cold or traumatic causes. It may also be developed in pyaemia, typhus, and puerperal fevers and in pulmonary consumption, or result from extension of inflammation from the peritonaeum, psoas or iliacus muscles, caries of the vertebrae or pelvic bones.[53]

Bull collected from the literature reports of 67 cases, of which 32 were fatal. He studied the ways in which the abscess resolved naturally, finding that the most common exit was through the abdominal wall (28 cases), and then into the cecum (15 cases). The key to successful treatment was mild treatment of the typhlitis or inflammation of the appendix that had existed prior to rupture, using leeches, opium, and rest with a minimal diet, hoping for resolution without suppuration. Once suppuration occurred, it was encouraged with warmth, poultices, etc, and the patient was then operated upon using the Parker method. Bull thought there were six surgical cases in the literature—three from Germany, Weber's, Burge's, and one of Parker's original four (he had missed three of Parker's cases). Five of these patients recovered; one German patient died.

Finally, Bull pointed out by implication that his was a clinically driven nosography. "Brief reference should be made to those cases of perforation of the appendix which are followed directly by general peritonitis. Such are by no means uncommon . . ."; but since death in 24 to 72 hours was the result and there was no circumscribed abscess, they fell into some different category, even if pathologically related to perityphlitis from perforation of the appendix. Bull's description of perityphlitis reflected medical opinion as exemplified in Roberts Bartholow's review, but may have been influenced by Henry Sands' pathological experience as well. At the July 8, 1957 meeting of the New York Pathological Society, Dr Sands presented a specimen of ulceration of the appendix which resulted in peritonitis and the death of the patient. The patient had also suffered from typhoid fever and Sands raised the question of whether other than an accidental relationship existed between the two. There were cases of foreign bodies found in the appendix after death which had done no harm; what was the relationship of ulceration to other conditions generally?[54]

In 1874 Sands reported his first independent case of perityphlitis for which he performed an operation. He cut down to the fascia, then inserted a trocar to drain the abscess. The patient recovered. But Sands was hardly alone; 1874 saw the presentation of numerous cases by a wide variety of practitioners. Samuel Ward,[55] surgeon to the Presbyterian Hospital, and Ernst Krackowizer,[56] a surgeon on both the Bellevue and New York Hospital staffs, reported cases of abscesses they had incised in 1872. However, there had been sufficient discussion to spread the idea beyond the elite hospital practitioners; and while reports by Gurdon Buck[57] and Charles Kelsey[58] and the operative experience of Professor James Wood (three cases reported by Buck)[57] were important to the progress of the subject, there are three reports of greater historical interest.

On December 31, 1873, Samuel Whitall was called to see an eight-year-old boy who had been vomiting for a day. Dr Whitall diagnosed "holiday indisposition" and prescribed a cathartic and light diet. On December 1, the boy, Simon, complained of pain in his right leg and lower abdomen with some tenderness upon pressure; however, the lack of tumefaction or marked localized tenderness—Gurdon Buck's sign of deep abscess—convinced Dr Whitall that the symptoms were muscular. By December 7 Simon "was not doing at all well" and a "circumscribed induration could be distinctly felt to the outer side of the caput coli and extending upward a short distance along the outer border of the colon." Whitall suspected perityphlitis, and gave castor oil to eliminate impaction from the differential. When it "operated freely" without any

change in the patient's condition, he concluded that Simon suffered from "perityphlitis with possible perforation of the appendix vermiformis. . ." He "determined to resort to the precautionary operation proposed by Dr. Willard Parker in 1865."

In fact Whitall used Weber's modification of the Parker operation, cutting down to the transversalis fascia. When no pus escaped through an "exploratory needle," he waited for the abscess to rupture the fascia. Whitall[49] found the operation relieved pain caused by the pressure of the abscess and in general the success of the procedure illustrated "the advantages and the safety of the operation."

A second case, in October 1874, resulted in perforation of the appendix and the patient's death within a week from generalized peritonitis. Sands had been called in for consultation but in a discussion after the postmortem "remarked that the case presented none of those physical signs in the shape of circumscribed abscess which were considered as sufficient to call for operative interference."[59]

By 1874, at least in the New York area, the Parker operation for drainage was becoming increasingly common. Without circumscribed abscess, however, the operation could not be condoned. Lister's idea of antisepsis still had not made much headway in America and even with antisepsis, abdominal procedures were risky. A third 1874 report indicates that Lister's ideas were having some impact in the management of local inflammation.

The third event of note was the occurrence of pain in the right iliac fossa and hip of a 15-year-old girl whose family physician was J. H. Pooley. Within a week swelling was prominent and after two weeks Dr Pooley recommended surgery; the parents would not consent. Finally, after three weeks, the child was operated upon and recovered. Pooley, a student of Parker's and a physician in Yonkers, New York, served with Burge on the staff of St John's Hospital. In the closing days of 1874 he was convinced of the efficacy of the Parker operation in perityphlitis and he practiced irrigation with carbolic acid during the procedure. Pooley[60] commented, "if other cases occur to me, I shall confidently follow it until convinced to the contrary."

In the late 1870s and early 1880s the use of the incision for perityphlitis became increasingly common, and reports began to appear from around the country and in European journals.[61-65] For example, in 1875 Pooley moved to Ohio and became professor of surgery in the Starling Medical College. He continued to use and teach surgical drainage for perityphlitis in his new post. The issues that emerged in papers and discussions were accurate diagnosis, prognosis, and the safety of the operation.

Diagnosis was of course the first issue. Perityphlitis was clinical, secondary to some other pathologic entity. Female patients presented particular difficulty since it was almost impossible to differentiate perityphlitis from pelvic peritonitis, cellulitis, metritis, and phlebitis. Buck felt these difficulties made pathology less important and "further enforced the proposition that the *circumscribed sensitive* point indicates the exact location of the abscess.[63]

An abscess could be incised and drained safely particularly if, as another surgeon commented, you "shall treat the wound after the antiseptic plan of Lister. . . for the purpose of destroying the atmospheric germs with which it may become poisoned."[63]

In 1880 Sands described a personal experience of 26 cases which he divided into four classes:

1. Cases terminating in resolution, without evidence of suppuration. [10 of 26]
2. Cases of abscess, terminating in spontaneous recovery. [3 of 26]
3. Cases of abscess, treated by operation. [11 of 26]
4. Cases of abscess, unopened and ending fatally. [2 of 26][66]

Sands' experience was not chronologically divided. Several unoperated cases were reported from 1878–1879; the difference between cases was largely clinical, with perhaps some belief in differences in pathology. Most of the cases of the first class reached a climax between the fifth and eighth day—a climax indicated by "a decided fall in the pulse and temperature. . . and by a marked diminution of abdominal tenderness, pain and distension." Sands was cautious—"regarding the pathology of the cases now referred to, nothing very definite can be stated"—but clearly believed that at least some of these patients had nonappendiceal perityphlitis: "symptoms pointed to plastic inflammation of the connective tissue adjacent to the caecum as the proximate cause of the characteristic induration. . ." Sands did acknowledge the possibility of appendiceal origin, particularly since many cases that recovered spontaneously recurred later, with positive evidence of previous inflammation of the appendix found at operation or autopsy. All that could be said for sure was "the invariable occurrence of such disease on the right side can be explained only by reference to the caecum or its appendix as the starting point; and pathological anatomy has demonstrated that lesions of the appendix are relatively more frequent, as well as more dangerous, than those of the caecum itself."

Obviously the diagnostic and prognostic signs that differentiated this first class of patients from the others were important. Time was the first consideration. "Since many of them terminate favorably before the end of the first week, the question of the propriety of surgical intervention will often not arise. . ." However, the surgeon's clinical judgment was the real key: "the question of operation is one that cannot be settled by time alone, and that all the circumstances of the case should be carefully considered before resorting to a procedure which may be needless and possibly hazardous."

The potential hazard did not deter Sands when he felt surgery was necessary. In his second group, cases of abscess terminating spontaneously, he had been planning to operate when the rupture into the bladder or bowel made the operation unnecessary; all three patients recovered. In his fourth group, he only found the perityphlitic abscess at postmortem so in terms of clinical diagnosis, these cases fell into a separate category—general peritonitis—but they were included because of a growing trend among surgeons to report failures as well as success. For Sands[66] in 1880, those patients who had a perforation of the cecum or appendix which progressed to general peritonitis without first forming a circumscribed abscess were "as yet beyond the reach of art, and possess therefore a pathological rather than a surgical interest."

While Sands' paper of 1880 probably reflected opinions which were or soon would be shared by the majority of the medical profession, other ideas were being discussed. The older idea of perforation of the appendix as a discrete pathological condition—tuphlo-enteritis—continued to appear in the literature. Fitz[67] reported an autopsy of such a case before the Boston Society for Medical Observation in 1877, and the records of the Massachusetts General Hospital show a steady series of such cases in which Fitz recognized inflammation of the appendix leading to perforation, general peritonitis, and death.[2]

Much more interesting, at least in retrospect, was a monograph by Carl Edvard With of Copenhagen. Professor With studied inflammatory disease of the appendix and reported 30 cases of peritonitis appendicularis. He was sure that there was one disease, appendicularis, which had three different clinical manifestations: adhaesiva, localis, and universalis. Peritonitis appendicularis adhaesiva resolved under medical, expectant therapy leaving adhesions later found at autopsy; localis was characterized by local peritonitis and a primary abscess in the right iliac fossa—perityphlitis; universalis was general peritonitis, the result of either perforation of the appendix or the extension of localis.[68] With[69-71] continued to publish his ideas and an abstract appeared in London in 1880. His student, Herman Mynter,[72] practiced in Buffalo, New York, and introduced the idea into the American literature in late 1879. He appears to have had only limited influence until after Fitz published his report on appendicitis in the late 1880s.

Surgical Management of Peritonitis

A new idea was introduced in 1880 when Herring Burchard[73] presented four cases of typhlitis (no circumscribed abscess preceding the general peritonitis) before the New York Academy of Medicine; all ended fatally but Dr Burchard still asked, "Is this disease necessarily fatal?" He thought not, even though "all hopes from the use of medicinal agents have been buried in the uniformly fatal termination of the disease." He suggested "that by a timely interference, there is a reasonable hope of saving a certain proportion of lives." By analogy he reasoned that while numerous cases of traumatic perforation of the intestine occurred, many times people with such serious wounds recovered. Burchard advised his colleagues that he thought that the wound in the intestine at the appendix could be sewn up and the abdominal cavity washed out with antiseptic solution through a lateral posterior incision.

In 1880 the idea that the abdominal cavity could or would be intentionally opened during general peritonitis was almost unheard of, but in 1880 Robert Lawson Tait of Birmingham, England, issued a startling challenge to his surgical colleagues. He urged that in all acute abdominal conditions the abdomen be immediately opened, even in the face of peritonitis, and in chronic cases where diagnosis was difficult he suggested exploratory surgery.[74] Tait's vast experience in gynecological surgery in Birmingham had convinced him that it was wrong to delay the laparotomy since the patient became progressively weaker and less able to withstand the surgery or to fight for recovery. Tait enjoyed comparative success and a very low postoperative mortality rate despite his opposition to Lister's techniques of antisepsis.[75] It would be ten years (1890) before Tait[76] would publish a report of an appendectomy he performed in 1880, so while his general suggestion, or "Tait's Law," as American surgeons would name it, was important he was not frequently cited in the appendicitis literature.

FIGURE 6. R. Lawson Tait (1845–1899). British surgeon and pioneer gynecologist; one of the earliest proponents of exploratory surgery in acute abdominal disease.

Tait's ideas would over time win the field but for the immediate future they were too radical and too dangerous for many practitioners, who easily recalled painful deaths of patients as a result of postoperative infections. The 1882 remarks of Robert Noyes, who was aware of the suggestions of Burchard and others that the surgeon interfere even if there are no indications of a localized abscess, are indicative of the general outlook in the early 1880s.

> I fail to find any recorded cases in which this procedure [laparotomy] has been attempted. However plausible and important this operation really is, the difficulty of certainty of diagnosis will stand an almost unsurmountable obstacle to its adoption. Medicine is useless in these cases except for the production of euthanasia and surgery cannot even accomplish this.[77]

Noyes was not an inexperienced or uninformed practitioner. His 1882 paper included a careful study of the literature and he had successfully operated on one case of perityphlitic abscess. While to some extent comparing apples and all fruit, he collected data to show a decline in

mortality as a result of the Parker operation. He recalled that William Bull in 1872 had collected 67 cases of perityphlitis, of which 32 were fatal, "a mortality of $47^{51}/_{67}$ percent." Of 100 cases of operation for perityphlitis, Noyes could find reported only 15 that had resulted in the death of the patient. "These statistics, showing a mortality of 15 percent in those cases treated by operation, and a mortality of $47^{51}/_{67}$ percent in those cases not so treated, sufficiently demonstrate that the prognosis is materially affected by the treatment."[77] In an era when the retrospective case controlled study was unknown such data were convincing—to some extent they still are.

Noyes recognized the difficulties that existed in the literature. First was the question of origins—

> Perityphlitis may result from exposure to cold, traumatism, or it may be idiopathic. It occurs occasionally in the course of phthisis, pyaemia and puerperal fever. But by far the greater majority of cases results from typhlitis or perforation of the posterior portion of the caecum, or of the appendix vermiformis.[77]

By typhlitis Noyes meant "an inflammation of the cecum and its appendix," which was believed to be the result of a prolonged functional disturbance of the cecum. The typhlitis could lead to perforation, either of the cecum or of its appendix.

> It is generally conceded that the appendix is responsible for the perforation in the great majority of cases of perityphlitic abscess due to this lesion [typhlitis]. . . The complete recovery in such a great proportion of cases of perityphlic abscess is presumptive evidence that the appendix. . . had been the site of the perforation. . . , for had the perforation been of the caecum, the recovery with fecal fistulae would have been more likely to have occurred.[77]

There were of course possibilities other than a perityphlic abscess in acute cases of typhlitis. Noyes believed he knew the pathological explanation of the clinical variations observed.

> The anterior portion of this viscus [caecum] and nearly the whole of the appendix are covered with peritoneum. Perforation of those portions of the caecum, or of the appendix caeci, covered with peritoneum results in general peritonitis, collapse, or if adhesions of the peritoneum have occurred, in an abscess having for its walls the peritoneum. Such an abscess is intraperitoneal and not perityphlitic; and it is important to bear this distinction in mind in the discussion of this subject, notwithstanding that the diagnosis between the two may well nigh be impossible, and notwithstanding that both are amenable to the same treatment.[77]

Noyes was aware of the frequent cases of recurrent symptoms of typhlitis in patients who developed abscesses as well as the fact that patients frequently had symptoms for several days before the development of an abscess. This explained the fact that most postmortems and numerous surgical observations implicated the appendix. "It is probable that many cases of perityphlitic abscesses result from perforation of the appendix. The serous investment of the appendix in these cases becomes adherent to the peritoneum in the iliac fossa, perforation here ensues and perityphlic abscess results."[77]

Noyes' remarks illustrate the difficulties and the progress of the early 1880s. There were clinically painful cases where no abscess was detected; there were cases where there was probably an abscess but it did not appear suppurative, at least it did not grow and suggest dangerous rupture; there were cases that required incision and in those surgeons were having very good results; finally, there were cases that seemed to result in peritonitis almost from the first hour, about which nobody could do anything. Noyes' explanations and others closely related to it took full advantage of the variety of the clinical symptoms, the pathological observations, the surgical progress, and the collected literature.[78] Noyes had every reason to be proud of the progress his profession had made and no reason to believe that radicals like Burchard were right.

Despite the reservations of probably the majority of practitioners there were surgeons who had the courage of their convictions. Antiseptic surgery had increased the margin of safety and it was clear that the patient with general peritonitis had little chance of survival without some immediate and drastic aid. There is no indication that American surgeons were the initial leaders in the surgical management of peritonitis, but they quickly took the suggestions of European innovators and argued in the American literature for their application. The chief portion of that literature considered the peritonitis which resulted from typhlitis. There is little question that the operative treatment of peritonitis began at the hands of men whose principal interest was gynecological surgery. As early as 1875 Tait operated for acute tubal infection, and in 1879 the French gynecologist Julien-Jean Julliard operated in the face of peritonitis, removing an ovarian cyst and relieving intestinal strangulation. In the early 1880s Tait and Julliard were supported by others in the new field of gynecologic surgery including John Homans of Boston, Peaslee of New York, and Spencer Wells, J. K. Thorton, and Arthur Keith of Britain.[75] They were soon followed by those we remember more as general surgeons, particularly Frederick Treves[79] of London and Johann von Mikulicz of Cracow.[80] There was of course a wide variety of levels of expertise in applying the surgical therapy in the early 1880s, but in all parts of the nation surgeons urged it as the best hope for a patient with peritonitis.[81-83]

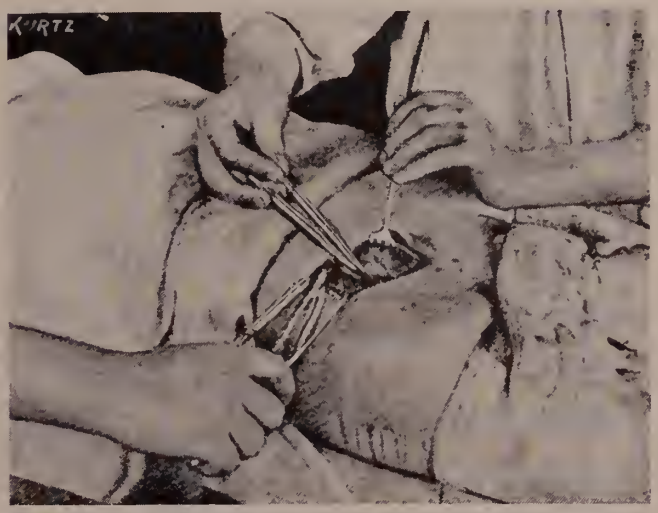

FIGURE 7. Incision operation for perityphlitis. An illustration from Arpad Gerster's *Rules of Antiseptic and Aseptic Surgery* (New York, D. Appleton and Co, 1888).

One hundred years later peritonitis remains a difficult problem, but it received national attention when at the 1881 American Medical Association meeting William A. Byrd of Quincy, Illinois, reported two cases of surgical intervention for perforation of the appendix with spreading peritonitis. Neither patient survived.[84] Other surgeons followed with similar results and some of course practiced it despite repeated failures.[85-88]

Retrospectively it is easy to see that one source of frustration to innovative surgeons of the 1880s was the belief that there were two diseases—typhlitis and perityphlitis (or in Sands' terms perforative peritonitis and perityphlitis). The confusion that surrounded their respective diagnoses raised the issue of who would drain the localized abscess before a general peritonitis developed. Physicians were apparently less than willing to adopt the surgical remedy, particularly in cases of typhlitis, and attempted medical treatments, many times until the patient was moribund. Without diagnostic precision based on pathological clarity there would be little improvement, for clearly there were cases in which the Willard Parker operation was of little value. However, following general peritonitis it was very difficult to be sure what the original source of the difficulty was. Perhaps at times the cecum was first involved and the appendix was destroyed as a secondary process. The techniques of the new science of pathology and in particular the results of studies of large numbers of patients would be necessary to resolve the problem.

In an 1884 paper Johann Mikulicz[89] described a successful operation for perforation of the intestine and an unsuccessful operation in which a perforation of the appendix was found at autopsy. He wrote, "had I investigated the neighborhood of the cecum by sight as well as by touch, the perforation of the appendix could not have escaped me and I should have excised it entirely, or closed the opening in the cecum with sutures. I am convinced that the peritonitis would have then subsided and the patient would have been saved." Mikulicz clearly had suspicions about perforation of the appendix, typhlitis, and perityphlitis; he certainly knew the work of Carl With, the British gynecologists, and the American surgeons who had perfected the Willard Parker operation.

> It is most important to understand the indications for it [laparotomy] in perforation of the appendix, as well as in typhlitis and perityphlitis dependent on the latter; and it is just here that we expect our experience in the future to set the matter in a new light. In this connection I cannot refrain from expressing my opinion that in severe cases of typhilitis and perityphlitis, even without perforation of the appendix, the therapeutic treatment hitherto employed should yield to operative. . . in any peritonitis the original cause of which is not clear, the region of the cecum should be investigated, and a possible perforation of the appendix considered.[89]

In the year and a half that followed the publication of Mikulicz's paper, R. U. Krönlein operated for peritonitis in three cases. In one case Dr Krönlein followed Mikulicz's advice and removed the appendix of a 17-year-old boy entirely, washed the intestines in antiseptic, and closed, but the boy died on the third day.[90] Because of the confusion of diagnosis it is impossible to know what caused the peritonitis (probably a perforated appendix) for which Barlow and Godlee[91] made an exploratory incision in 1885, drained the cavity with a second incision, and saw their patient recover. Krönlein[90] reported a similar success without the use of drainage. By the mid-1880s the stage was clearly set. Surgical therapy had made great strides, and several authors had suggested that all the clinical findings were related to disease of the appendix. No one, however, had yet managed to convincingly synthesize what was known.

FIGURE 8. Johann Mikulicz von Radecki, MD (1850–1905). Polish surgeon and a pioneer in aseptic surgery. He urged early operation in cases of acute abdomen.

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Disability evaluation

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The role of the physician is essential in the day-to-day operation of the $25 billion Social Security and Supplemental Security Income Disability programs.[1] In 1986 the Social Security Administration (SSA) will spend over $225 million for medical evidence, including $200 million for consultative examinations.[1]

No single definition of disability is universally accepted. Private insurance carriers operate under one definition, many large employers use another, and the Worker's Compensation program has its own. Under the SSA program, disability is strictly defined by statute as "inability to engage in any substantial gainful activity by reason of a medically determinable physical or mental impairment which can be expected to result in death or has lasted or can be expected to last for a continuous period of not less than 12 months. . . ."[2] Partial disability which is recognized in other benefit programs does not entitle an individual to receive Social Security disability benefits. The Social Security Act provides that a person's impairment must be so severe that he is unable to do any work available in the national economy. It does not matter whether such work exists in the immediate area in which he lives, whether a specific job vacancy exists for him, or whether he would be hired if he applied for work.[3]

"Disability" is also a legal term, whereas "impairment" is strictly a medical one. Therefore, treating physicians should not make legal statements concerning their opinions as to a patient's disabled status. Rather, they should objectively present the factual information concerning the patient's degree and type of impairment. Allowance or denial of a disability claim is made by Office of Disability Determinations personnel (a team comprising a physician and a professional analyst) using the program's established criteria. Thus, treating physicians should make their patients aware that they do not take part in the decision making process in regard to granting or denying disability benefits and that the medical evidence submitted by the treating physician is a statement of medical *facts* from the patients' records.

Medical criteria for impairment have been categorized into 13 body systems. These criteria are frequently reviewed and revised to keep pace with current medical knowledge of diagnosis and treatment methods. Approximately 80% of all claims involve only five of the 13 body systems (mental and neurological, 44%; cardiovascular, 12%; musculoskeletal, 19%; respiratory, 6%).[4]

The information needed for evaluation and decision making in regard to impairments of any type is related to two objectives:

- Verifying the diagnosis (based on an adequate history, physical findings, laboratory tests, and x-rays), and
- Assessing the severity based on all obtainable facts.

Outlined below are the medical facts needed for adequate assessment of impairments in the five most commonly involved body systems.

MUSCULOSKELETAL SYSTEM

In regard to musculoskeletal impairment, the information to be obtained should include a description of the joint(s) (eg, swelling, tenderness, redness), ranges of motion of any involved joint as well as of pertinent noninvolved joints, condition of the musculature (atrophy, spasm), sensory or reflex changes, circulatory deficits, and x-ray abnormalities. The indications for any orthopedic appliances being used should be noted. The emphasis should be on remaining function based on objective findings rather than allegations or symptoms that are not medically determined.

The presence of pain may be a factor in establishing a diagnosis. Its effect on the evaluation of severity of impairment depends on the presence of objective findings consistent with the severity of the pain. Documentation should include a description of the character of the pain, its location, whether the pain radiates, factors that exacerbate or relieve it, prescribed treatment (including name, dosage, and frequency of any analgesics being used), and the typical daily activities of a patient. This should correlate with the findings at examination, ie, a description of the patient's gait, joint motion, and ability to sit, stand, bend, squat, walk, and perform fine and gross manipulations.

In spinal disorders, appropriate abnormal physical findings must be shown to persist on repeated examinations, despite therapy, for a presumption to be made that the severity will last or has lasted for a continuous period of 12 months.

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The documentation of fractures should include the clinical evaluation of healing (where feasible) as well as x-ray findings to aid in determining whether return to full weight-bearing or use of the limb will occur within 12 months of occurrence of the fracture.

Cardiovascular System

The presence of a cardiovascular impairment does not always imply an inability to work. Its severity and its effect on a patient's ability to function must be assessed. Severe cardiac impairment results from one or more of the following: (1) congestive heart failure (CHF), (2) ischemia, or (3) conduction disturbances and/or arrhythmias. Regardless of etiology, findings consistent with CHF (vascular congestion such as hepatomegaly, peripheral or pulmonary edema on clinical examination, x-ray findings of considerable cardiomegaly on a film of the left lateral chest, and electrocardiogram (ECG) results) must be described.

The term "cardiomegaly" has no quantitative significance. Cardiomegaly is almost invariably an indication of congestive heart failure, past or present, but is not necessarily a determinant of remaining functional capacity. The lateral chest x-ray, by providing a view of the horizontal distance between the heart and the spine, readily lends itself to easy measurement, so, though not particularly accurate, it is a rough, general guide to cardiomegaly. The clinical findings of CHF need not be present at the time of reporting but the current chest x-ray and ECG findings are required.

In ischemic heart disease, to assure that angina is heart-related and not due to another cause (eg, biliary tract lesion, esophagitis, hiatal hernia, peptic ulcer, pancreatitis, cervical arthritis, costochondritis), the following must be fully documented: the character of the pain, its location, whether it radiates, its duration (with and without medication), its frequency, exciting causes, and modes of relief (rest, nitroglycerin, passage of time, etc). Shortness of breath as an isolated finding is not considered an anginal equivalent. Prinzmetal's-type angina (with ECG findings) is an anginal equivalent. Resting ECGs obtained should be submitted for review.

The results of stress testing, which measures an individual's circulatory capacity, should also be submitted. Circulatory capacity is measured in metabolic units, or METs, which represent the basal O_2 requirement of the body at rest. The value of one MET is considered to be 3.5 mL O_2/kg/min. The higher the number of METs a person achieves by exercise, the greater the circulatory capacity. The most common form of stress test is the Bruce[5] protocol, in which the patient exercises continuously on a treadmill that progressively increases in slope and velocity at three-minute intervals. A continuous electrocardiogram is taken. The test is terminated when one of three events occurs: 85% of the maximum permissible heart rate is reached (220 minus the age of the patient), the patient cannot or will not continue because of various complaints or findings, such as a sudden fall in blood pressure, or the electrocardiogram shows ischemic ST segment changes.

A positive test is indicated when ECG changes occur at 5 METs or less. The residual function capacity is determined by changes over 5 METs, or by a lack of ECG ST segment changes. Strips should be adequately labeled indicating findings at 5 METs and above; the date and the protocol used should also be indicated.

Conduction disturbances and arrhythmias must be correlated with clinical manifestations such as syncope and documented by resting ECG, ambulatory electrocardiography, and symptoms and signs. It is important to show that any alleged fainting spells occur together with the rhythm irregularity. This may require the use of the Holter monitor or other device. If stress testing is performed using the Master two-step technique, the date, the number of trips performed, and the time needed to perform the test, as well as adequately labeled strips, should be submitted. For purposes of evaluation, angina must be present as well as confirmatory findings (present or past) of coronary insufficiency.

Respiratory System

Impairment in respiratory disease usually results from chronic recurrent infections (ie, bronchiectasis, asthmatic bronchitis, mycobacterial and fungal diseases) or pulmonary insufficiency (with hypoxemia associated with hypercapnia, as in chronic obstructive pulmonary disease, or hypocapnia, as in chronic diffuse interstitial lung disease). Recurrent, episodic attack must be documented as to both frequency and severity.

Sufficient history should be provided for longitudinal evaluation, indicating the frequency of severe attacks, the treatment given (intravenous drugs, inhalation therapy), the place of treatment (hospital, emergency room), the duration of treatment, and the result. Pulmonary insufficiency can, in most cases, be objectively documented by physical findings, x-ray, and spirometry, though arterial blood gas studies at rest and during exercise may be needed. Well-performed spirometry depends on many factors, including the condition of the patient at the time of testing, the type of apparatus used, its maintenance, the training and understanding of the claimant, the professionalism of the technician, the cooperativeness of the patient, and the actual review of the spirogram obtained. (A statement that the claimant has dyspnea and a spirogram tracing indicating poor pulmonary function are not sufficient for a finding of disability.)

Neurological System

Neurological impairments can be divided into three categories: convulsive disorders, brain tumors, and persistent disorganization of motor function. Convulsive disorders, regardless of etiology, are evaluated according to type, frequency, duration, and sequelae of seizures. A detailed description of a typical seizure is needed. In order to prove severity the physician must also demonstrate a persistence of seizures despite the patient's compliance with prescribed anticonvulsive treatment. Adverse effects of medication on ability to function are also considered.

Brain tumors are evaluated according to the presence and grade of malignancy. In histologically malignant tumors the pathological diagnosis alone will be the decisive criterion for severity and expected duration. The presence, location, and effect of any metastases are also considered. In benign tumors the severity and duration of the impairment will be determined on the basis of the symptoms,

signs, and pertinent laboratory findings following therapy.

Persistent disorganization of motor function is evaluated in regard to the degree of interference with locomotion and/or interference with the use of fingers, hands, and arms on a sustained basis. Range of motion deficits in the involved extremities, atrophy, spasticity, rigidity, and muscle weakness should be documented in sufficient detail to allow for an evaluation based on objective findings. Speech deficits and personality changes should be described when present.

Mental Disorders

The criteria for establishing the presence of mental disorders have been extensively revised to reflect the concepts and definitions in DSM-III.[6] Moreover, the four categories of impairment which previously constituted this entire section have been expanded into eight categories, namely: organic mental disorders; schizophrenia, paranoid and other psychotic disorders; affective disorders, mental retardation and autism; anxiety-related disorders; somatoform disorders; personality disorders; and substance addiction disorders. The new listings require consideration of the interaction between the mental impairment and its effects in work settings. However, treating physicians are crucial to the adjudication process. No decisions can be made with respect to allowing or denying benefits until all relevant data are reviewed. The logical source of this material is almost always the physician who treats the patient. The physician should be able to provide the type of data ordinarily found in a standard report, hospital chart, clinical notes, case summary, etc. Thus, the presenting complaint, the mental status examination, the psychiatric history, the course of treatment, the various hospitalizations, the response to medication, and, finally, specific details concerning current function (drug activities, social interaction, response to stress, performance in rehabilitative settings, etc), can all be used as the documentation necessary for a proper determination.

Additional considerations for adjudication include nonmedical factors such as the patient's age, education, training, and work experience. These play a part in those cases where the impairment is of a lesser degree of severity than the criteria entail. Where these vocational factors are considered adverse, a claimant could be awarded benefits despite a lesser degree of impairment. But, as above, a fair determination of a claim requires adequate data concerning the claimant's condition and for this the treating physician is very important.

Important Points

- In 1984, 6.3 million persons in the United States received Social Security disability cash benefits every month; about 10% of those resided in New York State.[1]
- The program endeavors to keep pace with medical science and changing technology.

All aspects of the physician's role are important in disability determinations, but most important is the physician's well documented report, which allows for fair and proper decisions.

It is well known that presumptions and inferences cannot replace factual data in the correct assessment of disability. Adequate documentation of impairment allows for the greatest percentage of correct decisions, which is the program's goal. Presumptions and inferences should be involved only when needed facts cannot be obtained and a decision by our office is required.

New York State physicians have a professional obligation to their patients to supply the facts available from records. In a great many cases these provide sufficient information for arriving at a decision without further investigation. Using the suggested approach in regard to the five body systems mentioned above will allow for a higher percentage of correct and timely decisions for the benefit of patients, and will obviate the need for repeated contacts with the physician.

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Guidelines for the protection of health care workers in caring for persons who have some form of HTLV-III/LAV infection*

PART I

Recommendations for Preventing Transmission of Infection with HTLV-III/LAV† in the Workplace

Introduction

The information and recommendations contained in this document have been developed with particular emphasis on health care workers and others in related occupations in which exposure might occur to blood from persons infected with HTLV-III/LAV, the "AIDS virus."

This document contains detailed recommendations for precautions appropriate to prevent transmission of all bloodborne infectious disease to people exposed—in the course of their duties—to blood from people who may be infected with HTLV-III/LAV. They emphasize that health care workers should take all possible precautions to prevent needlestick injury. The recommendations are based on the well-documented modes of HTLV-III/LAV transmission and also incorporate a "worst case" scenario, the hepatitis B model of transmission. Because the hepatitis B virus is also bloodborne and is both hardier and more infectious than HTLV-III/LAV, recommendations that would prevent transmission of hepatitis B will also prevent transmission of AIDS.

HTLV-III/LAV is transmitted through sexual contact, parenteral exposure to infected blood or blood components, and perinatal transmission from mother to neonate. HTLV-III/LAV has been isolated from blood, semen, saliva, tears, breast milk, and urine and is likely to be isolated from some other body fluids, secretions, and excretions, but epidemiologic evidence has implicated only blood and semen in transmission. Studies of nonsexual household contacts of AIDS patients indicate that casual contact with saliva and tears does not result in transmission of infection. Spread of infection to household contacts of infected persons has not been detected when the household contacts have not been sex partners or have not been infants of infected mothers. The kind of nonsexual person-to-person contact that generally occurs among workers and clients or consumers in the workplace does not pose a risk for transmission of HTLV-III/LAV.

HTLV-III/LAV-infected individuals include those with AIDS who are diagnosed by their physician(s) as having other illnesses due to infection with HTLV-III/LAV and those who have virologic or serologic evidence of infection with HTLV-III/LAV but who are not ill.

The recommendations that follow are based on the well-documented modes of HTLV-III/LAV transmission identified in epidemiologic studies and on comparison with the hepatitis B experience.

Comparison with the Hepatitis B Virus Experience

The epidemiology of HTLV-III/LAV infection is similar to that of hepatitis B virus (HBV) infection. Much that has been learned over the last 15 years related to the risk of acquiring hepatitis B in the workplace can be applied to understanding the risk of HTLV-III/LAV transmission in health care and other occupational settings. Both viruses are transmitted through sexual contact, parenteral exposure to contaminated blood or blood products, and perinatal transmission from infected mothers to their offspring. Thus, some of the same major groups at high risk for HBV infection (eg, homosexual men, IV drug abusers, persons with hemophilia, infants born to infected mothers) are also the groups at highest risk for HTLV-III/LAV infection. Neither HBV nor HTLV-III/LAV has been shown to be transmitted by casual contact in the workplace, contaminated food or water, or airborne or fecal-oral routes.

HBV infection is an occupational risk for health care workers, but this risk is related to degree of contact with blood or contaminated needles. Health care workers who do not have contact with blood or needles contaminated with blood are not at risk for acquiring HBV infection in the workplace. In the health care setting, HBV transmission has not been documented between hospitalized patients, except in hemodialysis units, where blood contamination of the environment has been extensive or where HBV-positive blood from one patient has been transferred to another patient through contamination of instruments. Evidence of HBV transmission from health care workers to patients has been rare. It has been limited to situations in which the health care workers exhibited high concentrations of virus in their blood (at least 100,000,000 infectious virus particles per mL of serum), and the health care workers sustained a puncture wound while performing traumatic procedures on patients or had exudative or weeping lesions that allowed the virus to contaminate instruments or open wounds of patients.

Current evidence indicates that, despite epidemiologic similarities of HBV and HTLV-III/LAV infection, the risk for HBV transmission in health care settings far exceeds that for HTLV-III/LAV transmission. The risk of acquiring HBV infection following a needlestick from an HBV carrier ranges from 6% to

* These guidelines are based on recommendations of the United States Public Health Service Centers for Disease Control. They have been edited by the Medical Society of the State of New York's Committee on Preventive Medicine from statements appearing in *Morbidity and Mortality Weekly Report* (*MMWR* 1985; 34:681-695; *MMWR* 1986; 35:221-223).

† The designation Human Immunodeficiency Virus (HIV) has been proposed recently as the appropriate name for Human T-Lymphotropic Virus Type III (HTLV-III) or Lymphodenopathy-Associated Virus (LAV) by a Subcommittee of the International Committee for the Taxonomy of Viruses.

30%. This is far in excess of the risk of HTLV-III/LAV infection following a needlestick involving a source patient infected with HTLV-III/LAV, which is less than 1%. In addition, all health care workers who have been shown to transmit HBV infection in health care settings have belonged to the subset of chronic HBV carriers who, when tested, have exhibited evidence of exceptionally high concentrations of virus (at least 100 million infectious virus particles per mL) in their blood. Chronic carriers who have substantially lower concentrations of virus in their blood have not been implicated in transmission in the health care setting. The HBV model thus represents a "worst case" condition in regard to transmission in health care and other related settings. Therefore, recommendations for the control of HBV infection should, if followed, also effectively prevent the spread of HTLV-III/LAV. Additional measures are indicated for those health care workers who perform invasive procedures (see Part II).

Routine screening of all patients or health care workers for evidence of HBV infection has never been recommended. Control of HBV transmission in the health care setting has emphasized the implementation of recommendations for the appropriate handling of blood, other body fluids, and items soiled with blood or other body fluids.

Transmission from Patients to Health Care Workers

Health care workers include, but are not limited to, nurses, physicians, dentists and other dental workers, optometrists, podiatrists, chiropractors, laboratory and blood bank technologists and technicians, phlebotomists, dialysis personnel, paramedics, emergency medical technicians, medical examiners, morticians, housekeepers, laundry workers, and others whose work involves contact with patients, their blood or other body fluids, or corpses.

Recommendations for health care workers emphasize precautions appropriate for preventing transmission of bloodborne infectious diseases, including HTLV-III/LAV and HBV infections. Thus, these precautions should be enforced routinely, as should other standard infection-control precautions, regardless of whether health care workers or patients are known to be infected with HTLV-III/LAV or HBV. In addition to being informed of these precautions, all health care workers, including students and house staff, should be educated regarding the epidemiology, modes of transmission, and prevention of HTLV-III/LAV infection.

Risk of Health Care Workers Acquiring HTLV-III/LAV in the Workplace. Using the HBV model, the highest risk for transmission of HTLV-III/LAV in the workplace would involve parenteral exposure to a needle or other sharp instrument contaminated with blood of an infected patient. The risk to health care workers of acquiring HTLV-III/LAV infection in the workplace has been evaluated in several studies. In five separate studies, a total of 1,498 health care workers have been tested for antibody to HTLV-III/LAV. In these studies, 666 (44.5%) of the health care workers had direct parenteral (needlestick or cut) or mucous membrane exposure to patients with AIDS or HTLV-III/LAV infection. Most of these exposures were to blood rather than to other body fluids. None of the health care workers whose initial serologic tests were negative developed subsequent evidence of HTLV-III/LAV infection following their exposures. Twenty-six health care workers in these five studies were seropositive when first tested; all but three of these persons belonged to groups recognized to be at increased risks for AIDS. Since one was tested anonymously, epidemiologic information was available on only two of these seropositive health care workers. Although these two health care workers were reported as probable occupationally related HTLV-III/LAV infection, neither had a preexposure nor an early postexposure serum sample available to help determine the onset of infection. One case reported from England describes a nurse who seroconverted following an accidental parenteral exposure to a needle contaminated with blood from an AIDS patient.

Precautions to Prevent Acquisition of HTLV-III/LAV Infection by Health Care Workers. The precautions represent prudent practices that apply to preventing transmission of HTLV-III/LAV and other bloodborne infections and should be used routinely.

1. Sharp items (needles, scalpel blades, and other sharp instruments) should be considered potentially infective and should be handled with extraordinary care to prevent accidental injuries.
2. Disposable syringes and needles, scalpel blades, and other sharp items should be placed in puncture-resistant containers located as close as practical to the area in which they are used. To prevent needlestick injuries, needles should not be recapped, purposefully bent, broken, removed from disposable syringes, or otherwise manipulated by hand.
3. When the possibility of exposure to blood or other body fluid exists, routinely recommended precautions should be followed. The anticipated exposure may require gloves alone, as in handling items soiled with blood or equipment contaminated with blood or other body fluids, or may also require gowns, masks, and eye-coverings when performing procedures involving more extensive contact with blood or potentially infective body fluids, as in some dental or endoscopic procedures or postmortem examination. Hands should be washed thoroughly and immediately if they accidentally become contaminated with blood.
4. To minimize the need for emergency mouth-to-mouth resuscitation, mouth pieces, resuscitation bags, or other ventilation devices should be strategically located and available for use in areas where the need for resuscitation is predictable.
5. Pregnant health care workers are not known to be at greater risk of contracting HTLV-III/LAV infections than health care workers who are not pregnant; however, if a health care worker develops HTLV-III/LAV infection during pregnancy, the infant is at increased risk of infection resulting from perinatal transmission. Because of this risk, pregnant health care workers should be especially familiar with precautions for preventing HTLV-III/LAV transmission.

Precautions for Health Care Workers During Home Care of Persons Infected with HTLV-III/LAV. Persons infected with HTLV-III/LAV can be safely cared for in home environments. Studies of family members of patients infected with HTLV-III/LAV have found no evidence of HTLV-III/LAV transmission to adults who were not sexual contacts of the infected patients or to children who were not at risk for perinatal transmission. Health care workers providing home care face the same risk of transmission of infection as health care workers in hospitals and other health care settings.

When providing health care service in the home to persons infected with HTLV-III/LAV, measures similar to those used in hospitals are appropriate. As in the hospital, needles should not be recapped, purposefully bent, broken, removed from disposable syringes, or otherwise manipulated by hand. Needles and other sharp items should be placed into puncture-resistant containers and disposed of in accordance with local regulations for solid waste. Blood and other body fluids can be flushed down the toilet. Other items for disposal that are contaminated with blood or other body fluids that cannot be flushed down the toilet should be wrapped securely in a plastic bag that is impervious and sturdy (not easily penetrated). It should be placed in a second bag

before being discarded in a manner consistent with local regulations for solid waste disposal. Spills of blood or other body fluids should be cleaned with soap and water or a household detergent. As in the hospital, individuals cleaning up such spills should wear disposable gloves. A disinfectant solution or a freshly prepared solution of sodium hypochlorite (household bleach) should be used to wipe the area after cleaning.

Precautions for Providers of Prehospital Emergency Health Care. Providers of prehospital emergency health care include the following: paramedics, emergency medical technicians, law enforcement personnel, firefighters, lifeguards, and others whose job might require them to provide first-response medical care. The risk of transmission of infection, including HTLV-III/LAV infection, from infected persons to providers of prehospital emergency health care should be no higher than that for health care workers providing emergency care in the hospital if appropriate precautions are taken to prevent exposure to blood or other body fluids.

Providers of prehospital emergency health care should follow the precautions outlined above for other health care workers. No transmission of HBV infection during mouth-to-mouth resuscitation has been documented. However, because of the theoretical risk of salivary transmission of HTLV-III/LAV during mouth-to-mouth resuscitation, special attention should be given to the use of disposable airway equipment or resuscitation bags and the wearing of gloves when in contact with blood or other body fluids. Resuscitation equipment and devices known or suspected to be contaminated with blood or other body fluids should be used once and disposed of or be thoroughly cleaned and disinfected after each use.

Management of Parenteral and Mucous Membrane Exposures of Health Care Workers. If a health care worker has a parenteral (eg, needlestick or cut) or mucous membrane (eg, splash to the eye or mouth) exposure to blood or other body fluids, the source patient should be assessed clinically and epidemiologically to determine the likelihood of HTLV-III/LAV infection. If the source patient has AIDS or other evidence of HTLV-III/LAV infection, declines testing, or has a positive test, the health care worker should be evaluated clinically and serologically for evidence of HTLV-III/LAV infection as soon as possible after the exposure, and if seronegative, retested after six weeks and on a periodic basis thereafter (eg, three, six, and 12 months following exposure) to determine if transmission has occurred. During this follow-up period, especially the first six to 12 weeks, when most infected persons are expected to seroconvert, exposed health care workers should receive counseling about the risk of infection and follow US Public Health Service (PHS) recommendations for preventing transmission of AIDS. If the source patient is seronegative and has no other evidence of HTLV-III/LAV infection, no further follow-up of the health care worker is necessary. If the source patient cannot be identified, decisions regarding appropriate follow-up should be individualized based on the type of exposure and the likelihood that the source patient was infected.

Serologic Testing of Patients. Routine serologic testing of all patients for antibody to HTLV-III/LAV is not recommended to prevent transmission of HTLV-III/LAV infections in the workplace. Results of such testing are unlikely to further reduce the risk of transmission, which even with documented needlesticks is already extremely low. Furthermore, the risk of needlestick and other parenteral exposures could be reduced by emphasizing and more consistently implementing routinely recommended infection control precautions (eg, not recapping needles). Moreover, results of routine serologic testing would not be available for emergency cases and patients with short lengths of stay and additional tests to determine whether a positive test was a true or false positive would be required in populations with a low prevalence of infection. However, this recommendation is based only on considerations of occupational risks and should not be construed as a recommendation against other uses of the serologic test, such as for diagnosis or to facilitate medical management of patients. Since the experience with infected patients varies substantially among hospitals, some hospitals in certain geographic areas may deem it appropriate to initiate serologic testing of patients.

Transmission from Health Care Workers to Patients

Risk of Transmission of HTLV-III/LAV Infection from Health Care Workers to Patients. Although there is no evidence that health care workers infected with HTLV-III/LAV have transmitted infection to patients, a risk of transmission of HTLV-III/LAV infection from health care workers to patients would exist in situations where there is both (1) a high degree of trauma to the patient that would provide a portal of entry for the virus (eg, during invasive procedures) and (2) access of blood or serous fluid from the infected health care worker to the open tissue of a patient, as could occur if the health care worker sustains a needlestick or scalpel injury during an invasive procedure. Health care workers known to be infected with HTLV-III/LAV who do not perform invasive procedures need not be restricted from work unless they have evidence of other infection or illness for which any health care worker should be restricted. (See Items 6, 7 and 8 under Part II for the restrictions indicated for health care workers who perform invasive procedures.)

Precautions to Prevent Transmission of HTLV-III/LAV Infection from Health Care Workers to Patients. These precautions apply to all health care workers, regardless of whether they perform invasive procedures: (1) All health care workers should wear gloves for direct contact with mucous membranes or nonintact skin of all patients and (2) health care workers who have exudative lesions or weeping dermatitis should refrain from all direct patient care and from handling patient care equipment until the condition resolves.

Management of Parenteral and Mucous Membrane Exposures of Patients. If a patient has a parenteral or mucous membrane exposure to blood or other body fluids of a health care worker, the patient should be informed of the incident and the same procedure outlined above for exposures of health care workers to patients should be followed for both the source health care worker and the potentially exposed patient. (For this type of exposure, see Part II.)

Serologic Testing of Health Care Workers. Routine serologic testing of health care workers who do not perform invasive procedures (including providers of home and prehospital emergency care) is not recommended to prevent transmission of HTLV-III/LAV infection. The risk of transmission is extremely low and can be further minimized when routinely recommended infection-control precautions are followed. However, serologic testing should be available to health care workers who may wish to know their HTLV-III/LAV infection status. The question of serologic testing of health care workers who perform invasive procedures is addressed in Item 5 of Part II.

Risk of Occupational Acquisition of Other Infectious Diseases by Health Care Workers Infected with HTLV-III/LAV. Health care workers who are known to be infected with HTLV-III/LAV and who have defective immune systems are at increased risk of acquiring or experiencing serious complications of other infectious diseases. Of particular concern is the risk of severe infection following exposure to patients with infectious diseases that are easily transmitted if appropriate precautions are not taken (eg, tuberculosis). Health care workers infected with HTLV-III/LAV should be counseled about the potential risk associated with taking care of patients with transmissible infections and should continue to follow existing recommendations for infection control to minimize their risk of exposure to other

infectious agents. The health care workers' personal physician(s), in conjunction with their institutions' personnel health services or medical directors, should determine on an individual basis whether the infected health care workers can adequately and safely perform patient-care duties and suggest changes in work assignments, if indicated. In making this determination, recommendations of the Public Health Service's Immunization Practices Advisory Committee and institutional policies concerning requirements for vaccinating health care workers with live-virus vaccines should also be considered.

Sterilization, Disinfection, Housekeeping, and Waste Disposal to Prevent Transmission of HTLV-III/LAV

Sterilization and disinfection procedures currently recommended for use in health care and dental facilities are adequate to sterilize or disinfect instruments, devices, or other items contaminated with the blood or other body fluids from individuals infected with HTLV-III/LAV. Instruments or other nondisposable items that enter normally sterile tissue or the vascular system or through which blood flows should be sterilized before reuse. Surgical instruments used on all patients should be decontaminated after use rather than just rinsed with water. Decontamination can be accomplished by machine or by hand cleaning by trained personnel wearing appropriate protective attire and using appropriate chemical germicides. Instruments or other nondisposable items that touch intact mucous membranes should receive high-level disinfection.

Several liquid chemical germicides commonly used in laboratories and health care facilities have been shown to kill HTLV-III/LAV at concentrations much lower than are used in practice. When decontaminating instruments or medical devices, chemical germicides that are registered with and approved by the Environmental Protection Agency (EPA) as "sterilants" can be used either for sterilization or for high-level disinfection depending on contact time; germicides that are approved for use as "hospital disinfectants" and are mycobactericidal when used at appropriate dilutions can also be used for high-level disinfection of devices and instruments. Germicides that are mycobactericidal are preferred because mycobacteria represent one of the most resistant groups of microorganisms; therefore, germicides that are effective against mycobacteria are also effective against other bacterial and viral pathogens. When chemical germicides are used, instruments or devices to be sterilized or disinfected should be thoroughly cleaned before exposure to the germicide, and the manufacturer's instructions for use of the germicide should be followed.

Laundry and dishwashing cycles commonly used in hospitals are adequate to decontaminate linens, dishes, glassware, and utensils. When cleaning environmental surfaces, housekeeping procedures commonly used in hospitals are adequate; surfaces exposed to blood and body fluids should be cleaned with a detergent followed by decontamination using an EPA-approved hospital disinfectant that is mycobactericidal. Individuals cleaning up such spills should wear disposable gloves. Information on specific label claims of commercial germicides can be obtained by writing to the Disinfectants Branch, Office of Pesticides, Environmental Protection Agency, 401 M Street, SW, Washington, DC 20460.

In addition to hospital disinfectants, a freshly prepared solution of sodium hypochlorite (household bleach) is an inexpensive and very effective germicide. Concentrations ranging from 5,000 ppm (a 1:10 dilution of household bleach) to 500 ppm (a 1:100 dilution) sodium hypochlorite are effective, depending on the amount of organic material (eg, blood, mucous, etc) present on the surface to be cleaned and disinfected.

Sharp items should be considered potentially infective and should be handled and disposed of with extraordinary care to prevent accidental injuries. Other potentially infective waste should be contained and transported in clearly identified impervious plastic bags. If the outside of the bag is contaminated with blood or other body fluids, a second outer bag should be used. Recommended practices for disposal of infective waste are adequate for disposal of waste contaminated by HTLV-III/LAV. Blood and other body fluids may be carefully poured down a drain connected to a sanitary sewer.

PART II

Recommendations for Preventing Transmission of Infection with HTLV-III/LAV During Invasive Procedures

Definitions

An *operative procedure* is defined as surgical entry into tissues, cavities, or organs for repair of major traumatic injuries in an operating or delivery room, emergency department, or outpatient setting, including both physicians' and dentists' offices. An *obstetric procedure* is defined as a vaginal or cesarean delivery or other invasive obstetric procedure where bleeding may occur. A *dental procedure* is defined as the manipulation, cutting, or removal of any oral or perioral tissues, including tooth structure, where bleeding occurs or the potential for bleeding exists.

Recommendations

There have been no reports of HTLV-III/LAV transmission from a health care worker to a patient or from a patient to a health care worker during operative, obstetric, or dental invasive procedures. Nevertheless, special emphasis should be placed on the following precautions to prevent transmission of bloodborne agents between all patients and all health care workers who perform or assist in invasive procedures.

1. All health care workers who perform or assist in operative, obstetric, or dental invasive procedures must be educated regarding the epidemiology, modes of transmission, and prevention of HTLV-III/LAV infection and the need for routine use of appropriate barrier precautions during procedures and when handling instruments contaminated with blood after procedures.
2. All health care workers who perform or assist in invasive procedures must wear gloves when touching mucous membranes or nonintact skin of all patients and use other appropriate barrier precautions when indicated (eg, masks, eye coverings, and gowns, if aerosolization or splashes are likely to occur). In the dental setting, as in the operative and obstetric setting, gloves must be worn for touching all mucous membranes and changed between all patient contacts. If a glove is torn or a needlestick or other injury occurs, the glove must be changed as promptly as safety permits and the needle or instrument removed from the sterile field.
3. All health care workers who perform or assist in vaginal or cesarean deliveries must use appropriate barrier precautions (eg, gloves and gowns) when handling the placenta or the infant until blood and amniotic fluid have been removed from the infant's skin. Recommendations for assisting in the prevention of perinatal transmission of HTLV-III/LAV have been published (*MMWR* 1985; 34:721–726, 731–732).

4. All health care workers who perform or assist in invasive procedures must use extraordinary care to prevent injuries to hands caused by needles, scalpels, and other sharp instruments or devices during procedures, when cleaning used instruments, during disposal of used needles, and when handling sharp instruments following procedures. After use, disposable syringes and needles, scalpel blades, and other sharp items must be placed in puncture-resistant containers for disposal. To prevent needlestick injuries, needles should not be recapped, purposefully bent or broken, removed from disposable syringes, or otherwise manipulated by hand. No data are currently available from controlled studies examining the effect, if any, of the use of needle-cutting devices on the incidence of needlestick injuries.
5. If an accident occurs during an invasive procedure that results in exposure of a patient to the blood of a health care worker, the patient should be informed of the incident, and previous recommendations for management of such exposures should be followed.
6. No health care worker who has exudative lesions or weeping dermatitis should perform or assist in invasive procedures or other direct patient care activities or handle equipment used for patient care.
7. All health care workers with evidence of any illness that may compromise their ability to adequately and safely perform invasive procedures should be evaluated medically to determine whether they are physically and mentally competent to perform invasive procedures.
8. Routine serologic testing for evidence of HTLV-III/LAV infection is not necessary for health care workers who perform or assist in invasive procedures or for patients undergoing invasive procedures, since the risk of transmission in this setting is so low. Results of such routine testing would not practically supplement the precautions recommended above in further reducing the negligible risk of transmission during operative, obstetric, or dental invasive procedures.

SUGGESTED CHANGE IN THE TERMINOLOGY OF THE AIDS VIRUS

The International Committee on the Taxonomy of Viruses recently recommended the use of the term "Human Immunodeficiency Viruses (HIV)" for the retroviruses believed to be the cause of the acquired immunodeficiency syndrome (AIDS). The *Journal* asks that future authors use this new nomenclature in their articles. It will be the *Journal's* policy to use the old terminology HTLV-III/LAV together with the new term HIV once at the beginning of an article during a transition period. Further information on the new nomenclature may be obtained in: *Science* 1986; 232:699 and *Nature* 1986; 321:10.

Editor

Staphylococcal pericarditis in a homosexual patient with AIDS-related complex

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The clinical presentation of purulent pericarditis has changed considerably. In the pre-antibiotic era, suppurative infection in the pericardium was associated with pleuropulmonary disease and overwhelming infection with gram-positive cocci. Since the advent of antimicrobial therapy, the presentation of this disease has changed. Boyle et al[1] in 1961, followed by Rubin and Moellering[2] in 1975, noted the occurrence of disease most often in debilitated patients, often with impaired host defenses.

We describe an episode of *Staphylococcus aureus* pericarditis in a lymphopenic, homosexual patient with generalized lymphadenopathy consistent with AIDS-related complex (ARC). To our knowledge, this is the first such reported case of purulent pericarditis occurring in this immunodeficient population. The progression of pericardial effusion to effusive-constrictive pericarditis and then to severe constrictive disease requiring total pericardiectomy is noted.

CASE REPORT

A 35-year-old homosexual man was admitted to the hospital with fever, pleuritic chest pain, and progressive dyspnea of one week's duration. Eight months prior to admission he was found to have generalized nontender adenopathy, lymphopenia, and a T-helper/T-suppressor ratio of 0.166, due to an absolute decrease in T-helper cells. He was subsequently shown to have antibody to human T-cell lymphotropic virus type III (HTLV-III) by Western blot assay (performed in the laboratory of Drs M. G. Sarngadharan and Robert C. Gallo at the National Cancer Institute, Bethesda, Md) and was believed to have a prodrome of the acquired immune deficiency syndrome (AIDS). He had had multiple homosexual partners and denied intravenous drug use. His medical history included hepatitis B and amebiasis.

Three weeks before admission, the patient noted throat soreness, cough productive of yellowish sputum, postnasal drip, increased facial fullness, and paranasal sinus pressure. Ten days before admission he became febrile and pleuritic substernal chest pain developed.

His lungs were clear to auscultation, and there was no pleuropericardial rub. Sinus roentgenograms revealed bilateral maxillary opacification, and empiric therapy with erythromycin was started. One week later, the patient complained of shortness of breath, and a pericardial friction rub was heard. He was referred to the emergency room for admission.

The physical examination on admission revealed moderate tachypnea, a blood pressure of 125/75 mm Hg, with 5–10 mm Hg pulsus paradoxus; heart rate, 125/min; and temperature, 38.6°C. Venous pulsations were 1 cm above the sternal angle without Kussmaul's sign. Rubbery, 1–2-cm anterior and posterior cervical, submandibular, axillary, and inguinal nodes were present. There were rales at the base of the right lung. A cardiac examination was remarkable for a three-component pericardial friction rub.

The hematocrit was 28%; the white blood cell count was 4,500/mm^3 with 83% neutrophils, 8% lymphocytes, and 9% atypical lymphocytes. Coombs' test, cold agglutinin, and mycoplasma complement fixation titers were all negative. Chest roentgenograms revealed bilateral, small pleural effusions, clear lung fields, and an enlarged cardiac silhouette. Except for sinus tachycardia, the electrocardiogram was not remarkable.

Echocardiogram on admission revealed a small pericardial effusion (Fig 1) with bilateral small pleural effusions. Thoracentesis guided by sonography was unsuccessful. Blood and urine cultures were negative.

FIGURE 1. Two-dimensional echocardiogram (precordial long axis view) demonstrates a small pericardial effusion. LA, left atrium; LV, left ventricle; pe, pericardial effusion; RV, right ventricle.

The patient was thought to have a postinfectious pleuropericarditis and was treated with indomethacin. The chest pain and fever abated. However, three days later fever recurred and, despite transfusions to correct anemia, marked tachycardia persisted.

On the 19th hospital day the patient's blood pressure was 105/70 mm Hg, with a pulsus paradoxus of 15 mm Hg; heart rate, 130/min; and jugular pulsations, 8 cm above the sternal angle. There was no increase in dyspnea. A repeat echocardiogram revealed a markedly increased pericardial effusion. A diagnostic pericardiocentesis produced 150 cc of purulent appearing fluid with a red bood cell count of 750,000/mm^3 and a white blood cell count of 511,000/mm^3. There were 96% neutrophils and 4% lymphocytes. The glucose level was 5 mg/dL; protein, 6.2 g/dL. Gram's stain demonstrated gram-positive cocci, and cultures grew *S aureus*. Numerous blood cultures before and after this procedure were negative. Since the patient was allergic to penicillin, intravenous vancomycin was given. Using sonographic guidance, an indwelling catheter was placed in the posterior pericardium and 1,500 cc of fluid was drained during the next two days. A pulsus paradoxus of

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10–20 mm Hg persisted, and jugular pulsations remained 5–10 cm above the sternal angle. Drainage decreased and became thick and tenacious. Although the patient had no chest pain, dyspnea returned, and he remained febrile to 39°C.

On the 25th hospital day, pericardiotomy and drainage via a subxyphoid approach revealed a thickened pericardium with seropurulent fluid and multiple adhesions, which were manually lysed. During induction of anesthesia, the systolic blood pressure dropped to 80 mm Hg; upon opening the pericardium the blood pressure immediately rose to 130/90 mm Hg. A 32 French catheter was left in place. The drainage persisted, yielding an additional 500 cc during the next day. However, drainage decreased concomitant with an increase in dyspnea, tachycardia of 145/min, blood pressure of 115/65 mm Hg, and a 15 mm Hg pulsus paradoxus. Two days later, a repeat echocardiogram demonstrated a 1-cm thickened pericardium and minimal pericardial fluid (Fig 2).

At cardiac catheterization, the heart rate was 150/min, and simultaneous right and left ventricular pressures were 22/13 mm Hg and 110/14 mm Hg, respectively. The cardiac output was 4.08 L/min (2.19 L/min/M^2), and stroke volume was 27 cc. These results confirmed a restrictive diathesis.

The patient then underwent complete pericardiectomy via a median sternotomy approach. Recuperation was rapid, and two weeks after surgery he was discharged from the hospital. He was afebrile, with a blood pressure of 118/75 mm Hg, pulsus paradoxus of 8 mm Hg, heart rate of 112/min, and jugular pulsations 4 cm above the sternal angle.

Three months after surgery, the patient had returned to work and was unrestricted in daily activities, although he became tired more readily. His blood pressure was 110/70 mm Hg without pulsus paradoxus, his heart rate was 88/min, and his neck veins were flat.

Discussion

This patient presented with a post-infectious pleuropericarditis. The preceding upper respiratory infection and his initial response to anti-inflammatory therapy are consistent with this diagnosis. Since he meets the criteria for ARC,[3] recent data suggest an alternative pathogenesis for the pericardial effusion. Fink et al[4] have reported the frequent occurrence of pericardial effusion in patients with AIDS. Three of the patients in their report developed cardiac tamponade, but none had evidence of pericardial infection. Unlike these patients, the patient described here suffered from purulent pericarditis. This most likely resulted from transient staphylococcemia. His course was complicated by the rapid development of cardiac tamponade that required emergency pericardial drainage. Despite pericardiotomy and high-dose antimicrobial therapy, his temperature and hemodynamic status remained abnormal. Finally, he required total pericardiectomy for constrictive pericarditis and control of infection. After this procedure his condition improved, and he is doing well more than six months after surgery.

FIGURE 2. Repeat two-dimensional echocardiogram 17 days later shows a thickened pericardium without evidence of pericardial effusion. p, thickened pericardium; LV, left ventricle; RV, right ventricle; LA, left atrium.

Prior studies have shown an increased incidence of purulent pericarditis in compromised hosts, probably reflecting the frequency of bacteremia, fungemia, contiguous foci of pulmonary infection, and coexistent malignant, vasculitic, or hemorrhagic pericardial effusions in these patients.[1,2,5] The recent documentation of pericardial effusion as one of the cardiac complications of AIDS warrants a heightened awareness of the possibility of secondary purulent pericarditis in this emerging population of immunodeficient hosts.[4] The profound suppression of T-cell macrophage-mediated immunity in AIDS results in frequent life-threatening infection with intracellular pathogens.[6] Studies of B lymphocyte function reveal significant abnormalities in humoral immunity as well.[7,8] Lane et al[8] found increased numbers of fully activated, spontaneously secreting, antibody forming B-cells in the peripheral circulation of patients with AIDS. This was associated with a corresponding decrease in resting, and partially activated precursor populations, decreased responsiveness to T-dependent (pokeweed) and T-independent (formalinized *S aureus*) mitogenic stimuli, polyclonal hypergammaglobulinemia, and defective response to specific stimulation with newly encountered antigens such as keyhole limpet hemocyanin.

The clinical relevance of these findings has been suggested by recent reports documenting impaired antibody response to immunization[9] or invading microorganisms, an increased attack rate for pneumococcal pneumonia,[10] and a significant incidence of bacteremic infections commonly associated with B-cell immunodeficiency states in patients with AIDS.[11] Thus, when these patients require in-hospital care and invasive procedures—including insertion of intravenous catheters with the inherent danger of bacteremia—non-T-cell opportunists should be anticipated[11] and, as shown in this report, close observation for subsequent purulent pericarditis is indicated.

It has been observed that the typical signs and symptoms of pericardial disease are often lacking in these circumstances,[1] and thus it is necessary to maintain a high level of suspicion and obtain repeat echocardiograms in order to make an early diagnosis. Once the diagnosis has been made, antibiotic therapy and aggressive drainage are indicated. Total pericardiectomy will frequently be required. This report raises the possibility that another population, those patients with ARC, may also be at risk for the development of pericardial effusion and subsequent purulent pericarditis.

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Lung abscess involving *Corynebacterium pseudodiphtheriticum* in a patient with AIDS-related complex

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Acute pulmonary disease is recognized as a frequent complication of immune deficiency,[1] and multiple, synchronous, or recurrent pulmonary infections are common in patients with acquired immune deficiency syndrome (AIDS).[2-4] We describe the occurrence of a lung abscess involving a rare pathogen, *Corynebacterium pseudodiphtheriticum*, in a patient with AIDS-related complex (ARC).[5] This is believed to be the second reported case of lung infection in humans involving the isolation of this organism and the first in the setting of ARC.

CASE REPORT

A 24-year-old male homosexual with a history of intravenous drug abuse was seen with a chief complaint of pleuritic pain over the anterior mid-chest. During the previous ten months, he had experienced recurrent episodes of cough with minimal sputum, intermittent fever, chills, weakness, fatigue, loss of appetite, and weight loss of about 10 kg. He had also been exposed to tuberculosis in the recent past.

The patient had a temperature of 101°F. Physical examination revealed evidence of oral candidiasis, cervical, axillary, and inguinal lymphadenopathy, a papular rash over the left forearm, hepatomegaly, and splenomegaly. There were diminished breath sounds, with a dull sound on percussion of the left lower chest, and a grade II/VI systolic murmur over the precordium.

A posteroanterior chest radiograph revealed a rounded infiltrate in the left mid and lower zones, as well as left-sided pleural effusion. A Gram's stain of the sputum showed numerous neutrophils; several cultures of the sputum grew sparse mixed flora. Acid-fast bacilli were not identified in sputum smears. Sputum samples submitted for mycobacterial and fungal culture yielded no growth. Blood cultures grew no organisms on repeated occasions.

Other pertinent laboratory data included the following: hemoglobin, 12.4 g/dL; hematocrit, 35.9%; total leukocyte count, 3,800/mm^3, with 5% band forms, 80% neutrophils, 11% lymphocytes, 3% monocytes, and 1% atypical lymphocytes. T-lymphocyte function studies yielded the following values: total T cells, 942/mm^3 (normal range, 1,040–3,581/mm^3); total OKT_4, 110/mm^3 (normal range, 537–1,571/mm^3); OKT_4, 11.7% (normal range, 31–59%); total OKT_8, 550/mm^3 (normal range, 235–753 mm^3); OKT_4/OKT_8 ratio, 0.2 (normal range, 1.2–3.8).

Cutaneous anergy panel tests revealed anergy to mumps, *Candida*, purified protein derivative, and *Trichophyton* antigens. Tests for hepatitis B surface antigen were negative, and for core antibody, positive. Titers for cytomegalovirus, herpes 1 and 2, and *Toxoplasma gondii* were negative; the titer for Epstein-Barr virus was increased, 1:80 (normal, 1:20). Serum chemistry analyses revealed the following: lactate dehydrogenase (LDH), 292 IU/L; serum glutamic-oxaloacetic transaminase, 57 IU/L; alkaline phosphatase, 128 IU/L; gamma-glutamyl transferase, 109 IU/L.

An abdominal sonogram disclosed splenic enlargement (15 cm), and a liver-spleen scintiscan revealed hepatosplenomegaly. Nonspecific vasculitis was noted on skin biopsy of the papular rash. Bone marrow biopsy was nondiagnostic.

The patient received intravenous crystalline penicillin G (2 million units every four hours) for ten days. No clinical improvement was noted, and intravenous clindamycin (600 mg every six hours) was given in addition to the penicillin G. A diagnostic thoracentesis was performed, and 20 mL of fluid was aspirated. Cultures of the pleural fluid (as described in the section on microbiologic studies) did not grow aerobic or anaerobic bacteria, fungi, or acid-fast bacilli. The pleural fluid was an exudate, with a total cell count of 45,000/mm^3 with 45% neutrophils and 55% mononuclear cells. The protein content was 4.9 g/dL; LDH, 506 IU/L; glucose, 81 mg/dL; and amylase, 63 IU/L.

Following the thoracentesis, a hydropneumothorax developed necessitating the insertion of a chest tube; subsequently, the lung expanded fully, but purulent fluid continued to drain through the chest tube. Additional samples of the pleural fluid did not grow bacteria or acid-fast organisms. A computed tomographic scan of the chest revealed a circumscribed infiltrate in the superior segment of the lower lobe of the left lung, with minimal left-sided pleural effusion. The chest tube was later removed. Within three weeks of intravenous clindamycin therapy, the patient seemed to improve and his fever subsided; however, there was no radiographic improvement.

The patient was discharged from the hospital on oral clindamycin, and he remained asymptomatic for two weeks. He then presented again with intermittent low grade fever, malaise, and a dry cough. Decreased breath sounds and dullness to percussion were observed over the left infra-axillary region. The chest radiograph showed an 8 × 8 cm circumscribed infiltrate in the superior segment of the left lower lobe, with few small airspaces within the infiltrate. Gram's stained smears of sputum showed many neutrophils. Bacteriologic tests of sputum and blood were again negative. Fiberoptic bronchoscopy did not reveal an endobronchial lesion. A bronchogram with selective injection of dye into the superior segment of the left lower lobe showed displacement of the bronchi by a mass lesion.

A preoperative diagnosis of lung abscess or infected bronchogenic cyst was made, and the patient underwent a left thoracotomy. A large abscess cavity was noted in the left lower lobe, and a left lower lobectomy was performed. The surgical specimen weighed 490 g and measured 19 × 12 × 6 cm. A large cavity, 3.5 × 1.5 cm, with ragged mar-

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gins and containing blood and purulent necrotic material was seen on the anterior surface. The cavity, which was surrounded by grayish-white, firm consolidated parenchyma, exuded pus on pressure through a secondary bronchus which entered the cavity. Microscopic sections showed necrosis of alveolar septae and bronchiolar walls, and there were numerous abscesses with contiguous neutrophilic infiltrates. Admixed with the neutrophils and more prominent in the inflammatory component were histiocytes with eosinophilic granular cytoplasm which contained numerous intracytoplasmic pink globules. These globules were periodic acid Schiff (PAS) positive and diastase resistant. Sheets of these histiocytes were present in focal areas (Fig 1). Lying within and around the cytoplasm of the histiocytes were gram-positive bacilli, demonstrated by the Brown and Brenn stain (Fig 2). Another prominent histologic feature was the presence of large alveolar cells and bronchiolar cells with enlarged nuclei and containing eosinophilic inclusions surrounded by a clear halo. These cells were morphologically consistent with cytomegalovirus infection (Fig 3). Areas of desquamative pneumonitis and organizing pneumonia were also seen. A focal, foreign body giant cell reaction with polarizable debris within the giant cells supported a history of drug abuse. Stains for acid-fast bacilli, silver stain, and Dieterle's stain were negative for any recognizable organism. The hilar lymph nodes showed reactive changes with sinus histiocytosis.

The patient received intravenous crystalline penicillin (3 million units every four hours) and nafcillin (1 g every six hours) for four weeks. His recovery from surgery was uneventful, and the patient was discharged from the hospital on the tenth day after surgery, following collection and culture of a percutaneous tracheal aspirate. He returned for regular clinic visits. Two months after surgery, he presented with a low grade fever and a cough. Bacteriologic studies were negative. A residual pleural effusion was noted, and the fever was attributed to the postoperative pleural reaction. On subsequent visits, seroconversion was noted, with positive findings for antibodies to cytomegalovirus.

Microbiological Studies. The lung tissue was macerated in 2 mL of sterile tryptic soy broth. The mixture was inoculated onto aerobic media (blood agar, MacConkey's agar, chocolate agar, and colistin nalidixic acid blood agar-CNA), anaerobic media (CDC anaerobic kanamycin vancomycin blood agar, CDC anaerobic phenylethyl alcohol blood agar plates, and chopped meat glucose broth), mycobacterial media (Lowenstein-Jensen medium and 7H9), and fungal media (Mycocel and Sabouraud dextrose agar). The aerobic and anaerobic media were incubated under appropriate conditions for 48 hours. The mycobacterial and fungal media were incubated for six weeks. The tracheal aspirate obtained after surgery was inoculated onto the aerobic and mycobacterial media in the same manner as described above.

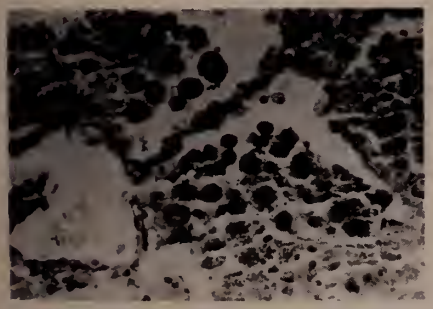

FIGURE 1. Histiocytes with eosinophilic granular cytoplasm containing numerous intracytoplasmic PAS-positive, diastase resistant granules (hematoxylin-eosin stain, original magnification × 400).

FIGURE 2. Gram-positive bacilli within the histiocytes (Brown and Brenn stain, original magnification × 400).

White, nonhemolytic colonies were recovered on CNA and chocolate agar plates. The organism, a gram-positive rod, was identified as *Corynebacterium pseudodiphtheriticum* based on positive reactions for catalase, nitrate, and urease. It was nonmotile and did not hydrolyze gelatin and esculin.[6] No mycobacteria or fungi were recovered. Viral cultures and cultures for *Legionella* sp were not performed. Pleural fluid obtained before surgery and processed as mentioned above did not contain aerobic or anaerobic bacteria.

Discussion

Significant pulmonary disease occurs in a majority of patients with AIDS.[2-4] Pneumocystosis, cytomegalovirus pneumonitis, atypical mycobacteriosis, and recurrent bacterial pneumonias are most frequently observed; pulmonary pathogens encountered less often include *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Nocardia* sp, *Coccidioides* sp, *Candida albicans*, and *Legionella pneumophila*. Infection caused by unusual pathogens is often seen in patients suffering from immunosuppression.[2-4]

In this patient with ARC,[5] the probable pathogen was a diphtheroid, *C pseudodiphtheriticum*. Although legionellosis could not be excluded by negative cultures and/or negative serologic studies, clinical response to crystalline penicillin G and negative findings on Dieterle's stain of histologic sections speak against that disease. *C pseudodiphtheriticum* was reported to cause disease in humans on ten previous occasions,[7-13] with only one case involving infection of the lung.[8] Of the ten cases, eight cases represented endocarditis in patients with prosthetic valves, or endocarditis involving valves scarred by prior rheumatic or congenital disease. Nathan et al[11] reported a case of malacoplakia with *C pseudodiphtheriticum* in a transplanted kidney, and the authors attributed the malacoplakia to infection with this organism. The first case of pneumonia in a human involving *C pseudodiphtheriticum* was reported by Donaghy[8] in 1983 in a patient with systemic lupus erythematosus. A striking feature in the case reported here was the finding of numerous histiocytes laden with PAS-positive, diastase resistant granules, in addition to the neutrophilic response. Bacilli were seen in the cytoplasm of these histiocytes. Michaelis Gutmann bodies, which are found in malacoplakia, were not seen.

C pseudodiphtheriticum is a normal commensal of the human nasopharynx.[14] It was probably first isolated by Van Hofmann in 1888 from the throats of humans.[6] Unlike other diphtheroids, these organisms show little pleomorphism, and they stain well and evenly except for a single transverse septum.[14] They grow well on all media, are inert towards carbohydrates, and hydrolyze and reduce nitrates.[15]

Diphtheroids are common inhabitants of the skin and mucous membranes. However, as reported by others, they can produce serious and even fatal infections in individuals with immunosuppression. Accounts of these infections have included suppurative lymphadenitis, osteomyelitis, meningitis, hepatic abscess,[16] and those described earlier.[7-13] Of particular interest in the context of this case is the letter by Sane

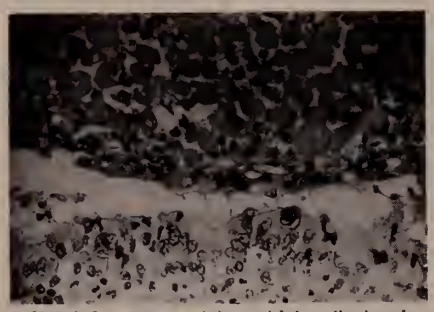

FIGURE 3. Enlarged bronchial cell showing eosinophilic intranuclear inclusion, consistent with cytomegaloviral infection (hematoxylin-eosin stain, original magnification × 400).

and Durack[17] which describes cavitating pneumonia caused by *Rhodococcus* (previously known as *Corynebacterium*) *equi* in a patient with AIDS. A similar case is described by Samies et al,[18] again in the setting of AIDS. *R equi* and *C pseudodiphtheriticum* essentially belong to the same group of normal commensals in the throat. It is important to emphasize that these commensals can become pathogenic in a setting of immunosuppression. The patient described here fell into two risk groups for AIDS, namely homosexuality and intravenous drug addiction. As more experience is gained with ARC and AIDS, we may detect increasing numbers of infections with such organisms. Thus, in a patient with AIDS or ARC, the potential pathogenicity of nondiphtherial coryneform bacteria should be recognized and, without clinical information, these isolates should not be discarded as mere contaminants.

Acknowledgment. The authors thank Ms Yvonne Arrocho for her secretarial help.

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Parenchymal calcification in hepatocellular carcinoma

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Intrahepatic calcification in adults is a relatively rare roentgenographic and histologic finding. The predisposing conditions include infectious diseases (tuberculosis, tertiary syphilis, and fungal and parasitic diseases), calculi, portal vein thrombosis, old hematomas, hemangiomas, and malignant neoplasms.[1–4] Among the malignant neoplasms that develop within the liver, metastatic mucous-secreting tumors calcify more frequently than primary hepatic tumors. Calcification in bile duct carcinomas[2,3,7] may be expected, since these tumors are mucous producing. In mixed mesenchymal tumors, calcification is common, since bone and/or cartilage are present as part of the mesenchymal elements.[2,8,9]

In contrast, calcification in hepatocellular carcinoma is unusual. A review of the English language literature dating back to 1950 reveals nine cases of calcified hepatocellular carcinoma in adults; the calcification was detected with either roentgenographic or histologic studies.[3,10–15] We report a case of hepatocellular carcinoma with radiologic evidence of calcification and a unique microscopic feature, showing the calcification within the tumor parenchyma, rather than in the stroma as reported in all other instances of calcification in hepatocellular carcinoma.

Case Report

A 64-year-old man was first admitted to the hospital in 1982 complaining of anorexia, an eight-pound weight loss, fatigue, increasing abdominal girth, and pain in the right lower quadrant. His medical history was significant for multiple blood transfusions during World War II and hepatitis which was diagnosed approximately 30 years ago. He worked as an astrophysical designer. He had a 100-pack/year history of cigarette smoking, drank little alcohol, and was not taking any medications.

The physical examination showed a cachectic man with diffuse spider angiomas, hepatomegaly, and ascites. Liver function studies were all within normal limits, except for slight elevations of serum glutamic-oxaloacetic transaminase and lactate dehydrogenase. Tests for hepatitis surface antigen were negative and for hepatitis surface antibodies were positive. The serum carcinoembryonic antigen (CEA) level was 1.2 ng/mL (normal, 0–5.0 ng/mL).

A chest radiograph was normal. An upper gastrointestinal radiographic series revealed psammomatous calcification in the right upper quadrant (Fig 1) as well as evidence of ascites. Serpentine folds in the esophagus with prominent gastric rugae suggested esophageal and possibly gastric varices. Abdominal sonography and a liver-spleen scan

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FIGURE 1. Upper gastrointestinal roentgenogram showing fine, closely packed clusters of calcium (arrow) in right upper quadrant.

revealed intrahepatic-space-occupying lesions and splenomegaly. A nodular liver with a mass in the right lobe was observed on laparoscopy. No tissue was obtained because of concern for bleeding. A subsequent percutaneous liver biopsy showed fibrous tissue infiltrated by anaplastic carcinoma of undetermined origin.

The patient was discharged on the 42nd hospital day and was to be followed by the Oncology Service. A repeat liver-spleen scan in January 1983 showed that the intrahepatic lesions were enlarging. The patient was readmitted to the hospital in May for therapeutic paracentesis and further evaluation of the liver tumor. During this hospital stay, his liver enzyme levels were approximately in the same range as on previous admissions, but the serum alpha-fetoprotein level was 114 ng/mL (normal, 25 ng/mL). Cytologic examination of the ascitic fluid showed cells that were highly suggestive of malignancy. On reevaluation, it was thought that the mass in the liver was probably a hepatic carcinoma. The patient's condition deteriorated rapidly before treatment was instituted, and he died on the 30th hospital day.

Autopsy Findings. Two to three liters of clear, greenish-yellow, exudative ascitic fluid were present. The liver weighed 1,700 g. The entire right lobe of the liver was shrunken and was mostly replaced by a pearly-white tumor with satellite nodules (Fig 2 top). The uninvolved hepatic parenchyma showed an irregular cirrhosis. On section, there was a large calcified area within the malignant tissue occupying approximately one third of the right lobe. The noncalcified tumor nodules were fleshy, bulging, and bile-stained. The gallbladder was not involved. Metastases were not found in other organs. Additional findings included splenomegaly (275 g) and esophageal and rectal varices.

On microscopic examination, the tumor was found to be composed of large eosinophilic, polygonal cells forming acini and trabeculae. Occasionally, the tumor cells also formed duct-like structures surrounded by fibrous stroma. Bile was seen within the lumen of some of the malignant acini. There was venous invasion and large areas of tumor necrosis. Calcification was observed within the cytoplasm of degenerating hepatocellular tumor cells (Fig 2 bottom), but little was seen in the fibrotic areas. The liver parenchyma not involved by malignancy showed irregular-sized regenerative nodules suggestive of posthepatitic cirrhosis. The histologic diagnosis of the neoplasm was hepatocellular carcinoma.

Discussion

Primary carcinomas of the liver are rare in the United States. Patton and Horn[13] reviewed the incidence in adults and found it to be 0.2-0.6% in six autopsy series, whereas Coleman et al[11] reported 0.1-2.3% in 11 series. Only Patton and Horn observed the presence of microscopic calcification in two of 60 hepatic tumors. Calcification becomes a significant feature if it can be detected by radiographic methods. Subsequently, several sporadic case reports of calcification in hepatic carcinoma were published. In some of these, the calcification was seen in mixed mesenchymal tumors[2,8,9] or in bile duct carcinomas.[2,3,7] Although infrequent, the intrahepatic calcification seen in these tumors was not unusual, since these tumors were known to calcify. In our survey of the English language medical literature, we found reported only nine adult cases of untreated hepatocellular carcinomas that showed calcification (Table I). The histologic diagnosis was made at postmortem, except in two cases in which the diagnosis was based on samples obtained from needle biopsies. The calcification was detected on radiographic studies in six cases. The patterns of calcification on radiograph were nonspecific and were described as flaky, diffuse, rosette-like, or as having radiating spicules. In those cases in which microscopic examination was performed, the calcification was present solely in the fibrous stroma.[13-15]

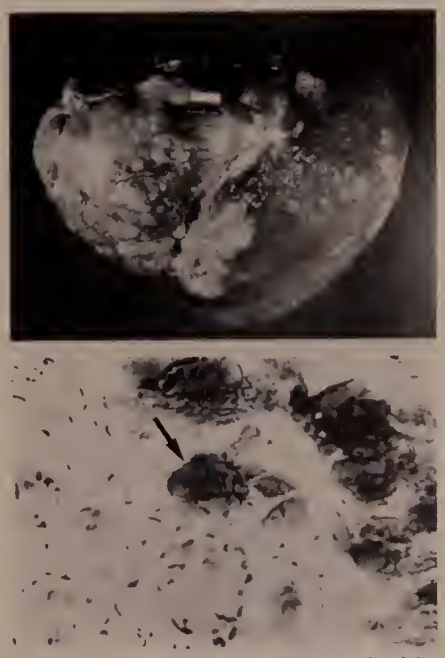

FIGURE 2. **Top,** calcified hepatoma in right lobe with satellite nodules in the left lobe. **Bottom,** dystrophic calcification in tumor parenchyma appearing as black crystalline material (arrow) in nests of degenerated hepatoma cells (hematoxylin-eosin stain, original magnification × 80).

In the case reported here, the radiographic findings portrayed the calcification as fine clusters of calcium—compatible with a malignant process such as that found with metastases from a mucous-producing adenocarcinoma of the ovary or colon. Unlike previous reports in which the calcification was present in the fibrous stroma, we found the calcification within the necrotic, malignant hepatocytes. Although this type of calcification (dystrophic calcification) occurs in various types of damaged tissues, it has not previously been reported to occur in the parenchyma of a hepatocellular carcinoma. This finding is the first documented report of extensive dystrophic calcification within the malignant epithelium of an untreated hepatoma.

With the increasing use of computed tomography, the frequency of detection of intrahepatic calcification will gradually rise. When this disorder is seen in association with cirrhosis, the diagnosis of hepatocellular carcinoma should be considered in the differential diagnosis. Following the administration of chemotherapy and/or radiotherapy, hepatocellular carcinomas also tend to calcify, as shown by two computed tomographic studies.[16,17] Although tissue samples were not available for histologic examination following the administration of therapy, one can assume that the calcification was probably secondary to tumor necrosis.

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TABLE I. Summary of Ten Cases of Calcified Hepatocellular Carcinoma in Adults (1950–1986)

Authors	Year Reported	Number of Cases	Patient Age	Patient Sex	Radiographic Description of Calcification	Histologic Diagnosis (postmortem)	Histologic Description of Calcification
Brick	1950	1	26	M	Small flecks in right upper quadrant	Hepatoma with cholangiomatous elements	Not reported
Coleman, Haines & Phillips	1954	1	67	M	Diffuse in right upper quadrant	Liver cell carcinoma, grade 2 (needle biopsy)	Not reported
Hunt	1963	1	28	M	Scattered densities	Cicatricizing liver cell carcinoma (needle biopsy)	Not reported
Patton & Horn	1964	2	Not reported		Not reported	Liver cell carcinoma	Small calcium deposits in stroma
Haddow & Kemp-Harper	1967	1	21	M	Spicules, sunburst-type, in right upper quadrant	Hepatocellular carcinoma	Not reported
Morgan et al	1972	2	40 21	M M	Rosette-like, diffuse	Poorly differentiated liver cell carcinoma	Calcium in necrotic fibrous areas
Moenander	1974	1	64	F	Calcifications radiating from center, right lobe (postmortem)	Hepatocellular carcinoma	Calcium in stroma
Chin et al	1986	1	64	M	Fine, closely packed clusters of calcium	Hepatocellular carcinoma	Calcium in tumor parenchyma

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Solitary diverticulum of the cecum

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Solitary diverticulum of the cecum is a rare entity that must be kept in mind when dealing with disorders in the ileocecal area. Potier[1] was the first to describe this lesion in 1912 in a 32-year-old woman. Mayo[2] in 1950 reviewed 202 cases of diverticula of the colon and, of these, only two were in the cecum. Diverticulitis of the colon usually produces no symptoms, unless complications occur. It is important to differentiate this disorder from acute appendicitis, carcinoma, and other less common diseases of the cecal region.[3] We report three cases that illustrate the clinical, laboratory, and pathologic features of this lesion.

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CASE REPORTS

Case 1. A 29-year-old man was admitted to the hospital for treatment of vague abdominal pain in the right lower quadrant of two weeks' duration, which suddenly increased in intensity one day prior to admission. The pain was accompanied by nausea, vomiting, and diarrhea. The pain was sharp and constant. It was localized to the right lower quadrant and extended to the pubic region.

The physical examination revealed tenderness, guarding, and rebound in the right

lower quadrant. The psoas sign was positive. The patient's temperature was 101.1°F. The white blood cell count was 20,400/mm^3 with 65% polymorphonuclear leukocytes.

A preoperative diagnosis of acute appendicitis and abdominal abscess was made. At surgery, the appendix was normal. A 4 × 3-cm hard nodular mass was found attached firmly to the outside of the cecal wall. An ileocecal resection and side-to-side anastomosis was performed.

Pathologic examination of the specimen revealed a normal appendix and a hemorrhagic indurated mass overlying the cecum, partially covered by purulent exudate. This mass contained a diverticulum communicating with a large pericecal abscess. This was confirmed by microscopic examination, which showed acute diverticulitis. The patient's recovery was uneventful.

Case 2. A 24-year-old woman was admitted to the hospital with sudden onset of suprapubic pain and anorexia. Ten hours after the onset, the pain became worse, radiating to the right lower quadrant. On physical examination, the abdomen was soft but markedly tender in the right lower quadrant and over the suprapubic area. The gynecologic examination was unremarkable. The patient's temperature was 99.8°F. The white blood cell count was 10,400/mm^3 with 82% polymorphonuclear leukocytes. The diagnosis was thought to be probable appendicitis or gynecologic disease.

At surgery, a mass was found in the lateral wall of the cecum. The appendix was normal. A right hemicolectomy with end-to-end anastomosis was performed.

Pathologic examination of the specimen revealed a thickened cecal wall and a cecal diverticulum. The microscopic examination revealed a normal appendix and an acute perforating diverticulitis with peridiverticular abscess formation. The patient's recovery was uneventful.

Case 3. A 27-year-old man was admitted to the hospital with diarrhea and mild cramping abdominal pain of four days' duration. The pain increased gradually and was localized in the right lower quadrant. There was mild nausea.

Physical examination revealed tenderness in the right lower quadrant, with moderate guarding. The patient's temperature was 98.7°F. The white blood cell count was 16,000/mm^3 with 71% polymorphonuclear leukocytes. A diagnosis of acute appendicitis was made. At surgery the appendix was normal. There was a 3-cm inflamed, indurated mass located within the anterior wall of the upper part of the cecum; the mass had the appearance of a diverticulitis. A right colectomy with side-to-end anastomosis was performed.

FIGURE 1. Histologic appearance of the cecal diverticulum, showing acutely inflamed wall (hematoxylin-eosin stain; original magnification × 5).

Pathologic study revealed a normal appendix. The serosa overlying the cecum was covered by fibrinous exudate. There was a large diverticulum which, on microscopic examination, showed acute diverticulitis and focal peritonitis (Fig 1). The patient's recovery was uneventful.

Discussion

Solitary diverticulum of the cecum is an uncommon disease. The youngest and oldest patients ever reported were seven and 72 years of age, respectively.[4] There has been no reported difference in the frequency of incidence between men and women.[9]

This disorder is usually asymptomatic, but inflammation or perforation can occur, and diagnosis is difficult. Most cases are misdiagnosed as acute appendicitis. The differential diagnosis may be helped by the observation that the pain starts and also remains in the right lower quadrant,[7] and that it may be of longer duration than is usually encountered in acute appendicitis. The lack of nausea, vomiting, and anorexia can serve as diagnostic aids,[8] but this has not been our experience. Physical examination is not particularly helpful in diagnosis. Radiographic visualization of a diverticulum by barium enema will help establish the definitive diagnosis.

On pathologic examination, these diverticula are usually found in an area 2 cm above to 1 cm below the ileocecal valve. Although they are generally solitary,[5] multiple cecal diverticula can exist.[6] A fecalith has been present in more than half of reported cases, and perforation has been reported in one third[9] of cases (in contrast with sigmoid diverticulosis). In structure, the specimens are true diverticula, having all intestinal muscle layers.

Cecal diverticulitis can be managed by medical means alone; antibiotic therapy and rest are all that would be required. However, the correct preoperative diagnosis is rarely made. Surgeons are hesitant to obtain a barium enema in the presence of an acute inflammatory process. If surgery is performed, any one of the following procedures may be employed: simple drainage; resection of the diverticulum; right colectomy when the local inflammatory reaction simulates malignancy. In each case the prognosis is excellent.

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Hard metal disease: A multidisciplinary evaluation of two cases

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Interstitial pulmonary disease caused by exposure to cobalt is known as hard metal disease. It is an occupational lung disorder first described in 1940 in German workers producing cemented tungsten carbide tools.[1] The principal manufacturing process involves mixing powdered metals, notably tungsten, titanium, and cobalt. These are subsequently formed under high pressure, heated in a furnace, and shaped into the final products—usually cutting or drilling tools or alloys of high strength and heat resistance. Other metals such as vanadium, tantalum, and niobium are also frequently used in this industry. Although interstitial pulmonary fibrosis is the main disease entity associated with inhalation of hard metals, other effects, including acute obstructive pulmonary changes and dermatitis, have also been reported.[2-4] Cobalt-related cardiomyopathy is a rare occurrence in industrial settings, in contrast to epidemics of cardiomyopathy related to heavy intake of beer contaminated with cobalt.[5-9]

We report on two patients with hard metal disease, emphasizing radiographic and cardiopulmonary findings as well as the results of tissue analysis for identification of the causative agents.

CASE REPORTS

Case 1. A 44-year-old man sought treatment for dyspnea on exertion of nearly 13 years' duration. Shortness of breath was first noted by the patient in early 1969. It was brought about by climbing one or two flights of stairs and was relieved by rest. On admission to the hospital in November 1982, the patient was short of breath after climbing one flight of stairs, hurrying on level ground, or going up a slight hill. The shortness of breath worsened during cold weather; then he had to stop for breath when walking on level ground, and used two or three pillows when sleeping. There was also a cough productive of grayish-yellow sputum. The cough had been nonproductive at the onset of his illness.

During the previous two to three years, nonradiating pain in the upper chest developed, and the patient experienced wheezing on a few occasions. Other symptoms experienced during the two years prior to admission included palpitation on slight exertion, throat soreness, symptoms of sinusitis, headache, and pain in the knee joints. A review of other systems was noncontributory. The patient's alcohol intake was moderate, and he denied cigarette smoking.

The patient started his working life in 1954 on an assembly line in a machine shop. In 1960 and during the following four years he held various jobs, one of which included sandblasting.

In 1965, the patient began working for a company that manufactured hard metal tools. In this position he handled tungsten carbide, cobalt, and other hard metals including tantalum, titanium, and niobium used in the manufacturing processes. His work involved sawing bricks made of hard metal compressed powder, grinding tools, cleaning the floor, and sieving the sweepings for reuse. He also blew excess dust from formed pieces at the furnace and sandblasted occasionally. He described these jobs and sites as "very dusty." He reported that there was inadequate ventilation during the early years of his employment. An exhaust system was subsequently installed, but its adequacy could not be determined from the patient's experiences. He rarely used protective respiratory equipment, but did use his own uniform, which he had to clean at home. He worked at the plant until 1969, and then had no further contact with hard metal dust. He was unemployed at the time of his admission to the hospital.

To investigate the shortness of breath, a chest radiograph was taken in 1969, which showed fine reticulonodular opacities consistent with interstitial lung disease. The patient underwent bronchoscopy, which showed bilateral, nonspecific bronchitis. Biopsies of the right scalene node and left lung were also performed.

Physical examination on admission was unremarkable. The chest radiograph taken at this time was interpreted as u 1/2 for small irregular opacities according to the ILO International Classification of Radiographs of Pneumoconioses, 1980[10] (Fig 1). Chest radiographs taken in early 1969, August 1969, and February 1982 showed similar abnormalities, but a chest film taken in March 1966 was not abnormal. A computed tomographic (CT) scan of the chest revealed interstitial lung disease, bullae and enlarged radiopaque (calcified) lymph nodes. Pulmonary function tests showed restrictive impairment indicated by reduction in forced vital capacity (FVC) (3.32 L, 63% of predicted value) and total lung capacity (TLC) (4.35 L, 56% of predicted value). Single breath diffusing capacity was moderately decreased (18.75 cc/min/mm Hg, 57% of predicted value). Maximum voluntary ventilation (MVV) was within normal limits (116.7 L/min, 83% of predicted value).

FIGURE 1. Chest radiograph from Case 1 showing the presence of small irregular, bilateral opacities, classified as u 1/2 according to the International Labour Office Classification of Radiographs of Pneumoconioses, 1980.[10]

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Pulmonary function tests performed in August 1969, October 1969, and May 1983 had also shown a restrictive type of dysfunction except for the MVV, which was reduced in 1969. Resting arterial blood gas levels determined in August 1969 were reported as being normal (P_{O_2}, 72 mm Hg; O_2 saturation, 94.4%; P_{CO_2}, 40 mm Hg; pH, 7.45). Resting O_2 saturation measured by ear oximeter in May 1983 was 91–92%.

In 1982, a review of the histopathology reports of 1969 indicated that the scalene lymph node biopsy was unremarkable. The lung biopsy showed focal interstitial and peribronchiolar fibrosis and chronic inflammatory infiltrates. Occasional eosinophils were noted among mononuclear cells, and large, dust-laden multinucleated cells were present in several air spaces. Numerous dust-filled, opaque macrophages were present in the lymphatic distribution around airways and vessels. No silicotic nodules were noted, and a search for asbestos bodies revealed one in the several sections available for review. The presence of an interstitial pneumonitis with the unusual multinucleated giant cells in air spaces best fit the rare histopathologic entity called giant cell interstitial pneumonia.[11]

Inorganic particles in the lung tissue sections were studied using scanning electron microscopy and energy dispersive x-ray quantitative analysis.[12] The concentration of exogenous particles was found to be 97 million per cubic centimeter of tissue; 95% were metal particles, with the vast majority containing tungsten. Some of them also contained titanium, niobium, and tantalum. Only one silica particle and two aluminum silicate particles were seen. Cobalt was not detected. This high concentration of particles suggested significant occupational exposure to these metals. A similar but nonquantitative analysis of the scalene node tissue showed some submicron particles containing tungsten.

Resting electrocardiography revealed a normal sinus rhythm of 72/min, with a normal axis of +20° and normal P-wave morphology, P-R interval, and QRS duration. M-mode echocardiography demonstrated mitral valve prolapse, but normal chamber dimensions and wall thickness. Gated blood pool scintigraphy revealed normal left ventricular function during rest and exercise. The apex of the right ventricle was hypokinetic both at rest and with exercise. At maximal exercise of 100 watts, a heart rate of 130/min and a blood pressure of 190/90 mm Hg were achieved.

Results of all other tests, including a complete blood count and differential, erythrocyte sedimentation rate, blood analysis, electrolyte levels, liver function tests, thyroid function tests, and urinalysis were within normal limits. The purified protein derivative test was positive (12 mm induration).

Case 2. A 39-year-old man was admitted to the hospital in November 1982 for evaluation of shortness of breath and cough, which he had had for approximately 13 years. His shortness of breath began in 1969 and had worsened progressively. It occurred mainly on exertion, such as while climbing more than one flight of stairs, but sometimes also when walking on level ground, and occasionally while at rest. He never experienced shortness of breath during the night. His cough was productive of greenish sputum in the early morning. There was no history of hemoptysis or chest pain. The patient also complained of infrequent wheezing, stuffy and running nose, dizziness, fatigue, and occasional palpitation during the two years prior to admission. He never smoked cigarettes.

A physical examination was unremarkable except for the patient's being slightly overweight. He had a history of occupational exposure to hard metal dust and fumes for approximately 17 years. Since 1965, he had worked as a machinist in the same factory as the patient described in Case 1. For five years, his main job was to grind compressed tungsten carbide pieces. There had been similar potential for exposure to tungsten carbide, cobalt, and other hard metals. Because of his chest condition, he was assigned, in 1969, to a supervisory job in the quality control department of the same factory, where he was exposed to less dust. He had no further exposure to hard metal dust after he was released from his job in early 1982. He was unemployed at the time of hospital admission. His work history was essentially confined to the cemented tungsten carbide industry.

The patient's medical history was notable for a hospital admission in 1970 for evaluation of a partially calcified solitary lesion in the right upper lung field, discovered on a chest radiograph taken in early 1968. Tomography showed increased lung markings bilaterally, especially in the right upper zone, in addition to the solitary lesion. Bronchoscopy showed evidence of bronchitis, and a culture was positive for *Pseudomonas* and *Proteus*.

An open lung biopsy was performed. Histopathologic examination of the 1.5-cm granulomatous lesion showed central calcification; the surrounding fibrous tissue was infiltrated with chronic inflammatory cells and foreign body giant cells. Staining revealed structures consistent with *Histoplasma capsulatum*. Examination of the lung tissue surrounding the lesion showed areas of slight perivascular and alveolar, septal collagenous fibrosis, with scattered areas of opaque pigment deposition. There were focal hyperplastic changes in the alveolar lining cells, and there was diffuse infiltration of the alveolar spaces with histiocytes laden with dark brown, sometimes refractile, pigment. Some of the intra-alveolar lining cells were the unusual multinucleated cells characteristic of giant cell interstitial pneumonia. The visceral pleura was edematous.

X-ray diffraction studies of the lung tissue indicated the presence of tungsten. The pigment in the histiocytes appeared to be carbon; however, tungsten could not be excluded by light microscopy. Quantitative microanalysis of a tissue section, performed as in Case 1, revealed a total concentration of exogenous particles of 780 million particles per cubic centimeter of tissue, of which 153 million per cubic centimeter contained tungsten. Associated titanium and tantalum were also noted. Cobalt was not detected.

The chest radiograph showed small irregular opacities in all parts of the lung fields, classified as u 1/1, according to the ILO International Classification of Radiographs of Pneumoconioses, 1980.[10] This finding was also noted on a chest radiograph taken in 1970. The chest radiograph from 1968, however, did not show this abnormality.

A CT scan of the chest performed during the 1982 hospital stay revealed radiopaque (calcified) mediastinal lymph nodes, interstitial lung disease, and posterior pleural thickening. Pulmonary function tests showed mild restrictive dysfunction manifested as slightly reduced FVC (4.28 L, 79% of predicted value) and total lung capacity (5.5 L, 77% of predicted value). The remainder of the tests, including forced expiratory volume in one second (3.64 L, 89% of predicted value) and MVV (188.24 L/min, 121% of predicted value), were normal. Single breath diffusing capacity was 27.62 cc/min/mm Hg, 82% of predicted value (normal). Previous pulmonary function tests performed in 1968 and 1970 had been normal. No arterial blood gas studies were performed.

Results of a complete blood count and differential, erythrocyte sedimentation rate, serum electrolyte levels, liver function tests, and blood studies were all within normal limits. A purified protein derivative test was negative.

The patient complained of palpitations and moderate dyspnea on exertion. Resting electrocardiography revealed a normal sinus rhythm of 66/min, with a normal axis of +50°, normal P-wave morphology, and a normal P-R interval and QRS duration. M-mode echocardiography demonstrated mild left ventricular hypertrophy. Resting left and right ventricular function were normal, as assessed by gated blood pool scintigraphy. Bicycle exercise in the supine position was performed, with the patient achieving a maximal heart rate of 150/min and blood pressure of 200/95 mm Hg. At peak exercise of 125 watts, left ventricular function augmented normally, while right ventricular function deteriorated.

Analysis of Dust Samples. Information about levels of airborne contaminants in the plant was not available, but samples of settled dust from various production areas in the facility were obtained. Eight dust samples were analyzed by transmission electron microscopy with an energy dispersive x-ray analyzer. This microchemical analysis, performed on individual particles as well as on fields of particles, provides information regarding the relative amounts of elements present.

All samples consistently showed a predominance of tungsten and cobalt. Iron was found in five samples. Silver was found in

seven samples, usually as a trace component. Titanium was found in two samples, while niobium was found in one sample. With the notable exception of cobalt, the dust particles were similar in size and composition to those particles analyzed in the lung biopsies.

Discussion

Hard metal disease is a potential hazard of exposure to cobalt in the cemented tungsten carbide industry. Although exposure to other metals such as tungsten, tantalum, titanium, and vanadium is common, it is believed that interstitial pulmonary fibrosis is a toxic effect of cobalt. It is noteworthy that similar, if not identical, disease is seen with cobalt exposure in other industries that lack the other hard metal components.[13] Acute and subacute pulmonary effects attributed to cobalt include asthma and fibrosing alveolitis.[14] The anamnestic, clinical, and histopathologic findings in these two patients represent the classical picture of hard metal disease, notably interstitial pulmonary fibrosis,[15] often showing the rare pattern characteristic of giant cell interstitial pneumonia.

In both patients, symptoms of the disease appeared relatively soon after the onset of exposure—after three and five years, respectively. This temporal relationship is common for hard metal disease[16] and differs from the longer latency periods characteristic of other pneumoconioses, such as asbestosis and silicosis.

The initial chest radiographic abnormalities, consisting of a pattern of diffuse interstitial lung disease, did not resolve when exposure ended (Case 1) or after attempts to reduce exposure (Case 2). This suggests that the disease was diagnosed, based on radiographic findings, at a subacute or chronic stage. Cobalt-related acute, obstructive airway disease, which frequently develops after several months of exposure, is associated with intermittent asthmatic symptoms and is usually not accompanied by radiographic abnormalities. Hard metal disease was confirmed by the histopathologic findings on lung biopsies. The granuloma noted in Case 2 was a distinct histoplasmotic lesion and was not related to the other histopathologic findings of interstitial fibrosis and giant cell interstitial pneumonia.

Cobalt has been identified by microchemical analysis in lung tissue of some workers with hard metal disease who were employed in the cemented tungsten industry.[16] It is of interest to note that cobalt was not detected in the lung tissue of the patients described in this report. In contrast to other hard metals, cobalt does not remain in the lung tissue for prolonged periods of time and can thereby escape detection. This can be explained in part by the greater solubility of cobalt in plasma than in physiologic saline solution. However, in earlier studies, the lower sensitivity of analytical methods for the detection of cobalt may also be a factor to consider.[16,17] The radiopaque, calcified lymph nodes noticed on the CT scan of the chest were a common finding in a group of hard metal workers we have examined.[18] Whether this represents a radiographic manifestation of hard metals accumulated in the lymph nodes was not directly determined in these patients, but studies by other investigators have demonstrated the accumulation of tungsten, tantalum, and cobalt in the mediastinal lymph nodes of workers employed in the cemented tungsten carbide industry.[3]

The myocardial effects of cobalt have been reported in connection with several epidemics of cardiomyopathy, which were related to the ingestion of beer containing cobalt used as an antifoaming agent. This cardiomyopathy was associated with evidence of severe left ventricular dysfunction and high mortality.[8,9] In contrast, few cases of cardiomyopathy with a fatal outcome have been reported among workers exposed to cobalt on the job,[5,6] although transient cardiac effects have been documented among workers who perform wet grinding of hard metal tools. S-T depression and T-wave changes were more common in an exposed population as compared to a control group. Differences in electrocardiographic (ECG) abnormalities between the workers and an unexposed control population disappeared when the workers were examined after a four-week holiday, indicating that ECG changes may be reversible.[19] However, no studies of ventricular function were reported in these subjects. The abnormality in right ventricular function observed at rest in one of the patients reported here and with exercise in both patients is most likely a manifestation of occult cor pulmonale rather than a cobalt-related cardiomyopathy.[20] Although this selective right ventricular dysfunction may occasionally be seen in right coronary heart disease, it is a common disorder in patients with pulmonary hypertension.[21-24]

The two reported cases also illustrate the importance of performing microchemical analysis of lung tissue in order to identify etiologic factors in interstitial pulmonary fibrosis. A complete occupational history can provide important clues to cause-effect relationships in cases of interstitial lung disease, but the demonstration of similarities between compounds found in lung tissue and those identified in the work environment strengthens the relationship. A more general application of such analytical techniques in cases of idiopathic interstitial lung disease may shed much needed light on the possible etiologic role of inorganic matter in this and similar conditions.[12,25-29]

The two patients reported here worked in the same plant. Our experience with these two patients and the concern voiced by coworkers have prompted us to evaluate the prevalence of hard metal disease among workers formerly employed in that factory, as well as in other facilities that process hard metals. A recent study of tungsten carbide production workers has also called attention to the continuing hazard of occupational overexposure to cobalt.[30]

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FROM THE LIBRARY

LEAD POISONING IN THE COMMUNITY

From the Standpoint of the Industrial Worker

Lead is encountered with great frequency in nonindustrial life. Attention has repeatedly been called to the fact that lead is present in practically all foods and fluids ingested. Such common foods as bread, fruits, vegetables, cereals, meats, candy, milk, eggs, fish, water, and common salt have been found to contain varying amounts of lead. The fact that lead is a natural constituent of the soil and occurs in the biological excreta of human beings, removed from industrial civilization, was shown by Kehoe and his coworkers in their very interesting studies in 1933.

The most frequent occurrence of lead poisoning in the nonindustrial population is found in children. The use of powder containing lead, on the body, the prolonged use of the lead nipple shield, the eating of unusual substances such as lead paint from cribs, toys, and chairs, have been responsible for the occurrence of lead poisoning in infants. Williams and his coworkers reported the occurrence of lead poisoning in a family following the use of battery casing for fuel purposes. An unusual case of lead poisoning in a child who developed peripheral neuritis, was reported by Goodwin. In the adult nonindustrial population, cases of lead poisoning following the use of snuff, wines and ciders, beer, toothpaste, and red pepper have been reported.

We have reviewed the records of two representative hospitals in the Borough of Brooklyn and have found that the diagnosis of nonindustrial lead poisoning in adults has never been made. It is probable that the records of other medical institutions would show the same results. Among children, however, the diagnosis of nonindustrial lead poisoning is not unusual in hospital practice.

From recent experimental observations, Kehoe and his coworkers found that the normal American adult excreted at the rate of 0.02 to 0.8 mgm. of lead per liter of urine and at the rate of 0.03 to 0.1 mgm. of lead per 100 gm. of ash feces. The main daily output of the normal individual varied from 0.05 to 0.38 mgm. The lead intake in the food of selected subjects was approximately equivalent to the lead content of their feces. This fact may be taken as evidence not only of the passage of a great proportion of ingested lead through the alimentary tract unabsorbed, but also of the predominant source of the lead which is absorbed and excreted by normal persons. It is reasonable, therefore, to assume that there is a daily constant intake of lead by all individuals whether or not they are exposed to this heavy metal in their occupation. A diagnosis of plumbism is seldom made or considered in the absence of typical symptoms of lead intoxication, especially when there is no history of occupational exposure. . . .

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Physicians and medical malpractice

TO THE EDITOR: I would like to commend the *Journal* on the publication of its special thematic issue on medical malpractice. The various articles present a comprehensive, scholarly treatment of the subject. I found Mr Charles Kramer's excellent article (1986; 86:348–351) of special interest: It presents views that differ from some of those presented in the other articles, but its inclusion provides the issue with balance and perspective. I do not have to agree with every point in order to acknowledge the overall correctness of Mr Kramer's position.

We physicians inherently believe in our constitutional system, respect the law, and seek to understand the special nuances that apply to our profession. We do not defend malpractice, and I am certain that Mr Kramer is embarrassed by examples of frivolous lawsuits on the part of his fellow attorneys. Where we all do ourselves an injustice is in attempts to simplify matters by dividing the participants of a risk dispute into "good guys" and "bad guys," rather than focusing on the *problem* and considering all involved as having complex and interacting motives. It is clear that when hospital funds must be diverted to support malpractice and risk management, the institution's ability to maintain quality patient care, education, and research is seriously compromised.

I think that the time has come for some of us to start rebuilding the bridges between the legal and medical professions. This country was built on the intellectual abilities, idealism, and dedicated efforts of its professionals.

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Medical malpractice

TO THE EDITOR: I have read with interest the article, "Medical malpractice: The patient's point of view" (1986; 86:348–351). I am particularly interested in the statement that "a hospital is obliged to carry out the physician's orders and cannot substitute its own ideas even though by doing so it is following customary practice." I would appreciate knowing what the legal basis is for the affirmation of this principle.

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In reply. The basis of the statement, "a hospital is obliged to carry out the physician's orders and cannot substitute its own ideas even though by doing so it is following customary practice," comes from a decision of the Court of Appeals, the highest court in this state. The case is *Toth v Community Hospital*, 22 NY2d 255, 1968.

The case involved a pair of twins who were born prematurely in 1953 and became blind as a result of retrolental fibroplasia (RLF). The action was against the pediatrician and the hospital. The doctor had ordered that four liters of oxygen be given per minute. The nurses gave six liters, which was the accepted practice at the time. However, oxygen was already suspected of being implicated in causing RLF.

The court in its decision stated at p 265:

> The primary duty of a hospital's nursing staff is to follow the physician's orders, and a hospital is normally protected from tort liability if its staff follows the orders. Nevertheless, if the doctor's orders are to be a hospital's shield from tort liability, it cannot at the same time maintain that a deviation which causes injury cannot be a basis for tort liability because other physicians or medical institutions might consider the treatment actually given as acceptable. More important than the question of logical consistency is the issue of social policy. There is every reason to encourage the hospital staff to carry out diligently the doctor's orders while there are not countervailing considerations which would justify relieving the hospital from tort liability for failing to do so.

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Mediastinal veno-occlusive disease associated with herbal tea ingestion

TO THE EDITOR: Bush teas incorporate plants of the *Seneco*, *Crotalaria retusa*, and *Heliotropium* species. In certain societies, bush teas are thought to be endowed with medicinal properties and are used in the treatment of fevers and respiratory problems. Unfortunately, pyrrolizidine alkaloids in these teas can produce hepatic veno-occlusive disease. Cardiopulmonary changes similar to those involving the liver have been reported.[1,2] We describe a patient from Trinidad with a history of herbal tea ingestion in whom fibrosis of the superior vena cava developed that required bypass surgery.

Case Report. A 59-year-old man first noticed swelling in his chest 20 years prior to seeking treatment. It had become more severe in the past two and a half years, accompanied by painless swelling of the neck and shoulders. He complained of dyspnea on exertion or emotional stress, and occasional paroxysmal nocturnal dyspnea. Recently, blurred vision, headaches, and dizziness upon bending down had developed. There was no history of heart disease, asthma, or tuberculosis, but the patient had been diagnosed as having recurring bronchitis, which was treated regularly with "bush tea" as a homeopathic remedy. The patient suffered from hypertension and had suffered pneumonia in April 1984. He had not smoked or ingested alcohol in the past 15 years.

On physical examination, the patient was in no apparent distress, with 2+ edema of his neck and chest, accompanied by multiple dilated venous varicosities of the chest, abdominal wall, and upper extremities; the remainder of the examination was unremarkable. The patient had been referred to the Albany Medical Center by his physician in Trinidad for evaluation and treatment.

Chest roentgenography revealed a widened mediastinum with increased bilateral

markings suggesting mild fibrosis. Bilateral venography demonstrated significant tortuosity of superficial chest vessels and of the right subclavian vein, accompanied by filling defects of the right internal jugular and left innominate veins. The superior vena cava was occluded (Fig 1). Bronchoscopy disclosed diffuse bronchitis and submucosal venous engorgement. Results of a purified protein derivative test were negative, and bronchial cultures for bacteria, mycobacteria, and fungi were negative.

Bypass of the superior vena cava from the right internal jugular vein to the right atrium was performed using a spiral saphenous vein graft, as described by Doty.[3] At surgery, extensive fibrosis was found occluding portions of the right internal jugular and left innominate veins, the superior vena cava, the left superior pulmonary vein, and the superior atrio-caval junction.

Intra-operative biopsy of the affected vessels revealed medial fibrosis with mural sclerosis and calcification. The lungs showed focal interstitial fibrosis and medial hyperplasia of the small arteries. Atrial tissue removed to implant the bypass conduit demonstrated hypertrophy of muscle fiber with chronic inflammation.

Discussion. Most reported cases of hepatic veno-occlusive disease associated with pyrrolizidine alkaloid ingestion are from the West Indies and the Far East. Signs and symptoms of acute, subacute, and chronic disease are well established. Stuart and Bras[1] described four cases with pulmonary involvement. In three of these, pulmonary signs and symptoms accompanied hepatic congestion. Pleural effusion has been attributed to either leakage of ascites through diaphragmatic lymphatics or a hypoproteinemic state secondary to cirrhotic changes of the diseased liver. These explanations, however, would not account for cases in which the protein content was unusually high or in which pleural manifestations preceded hepatic symptoms.

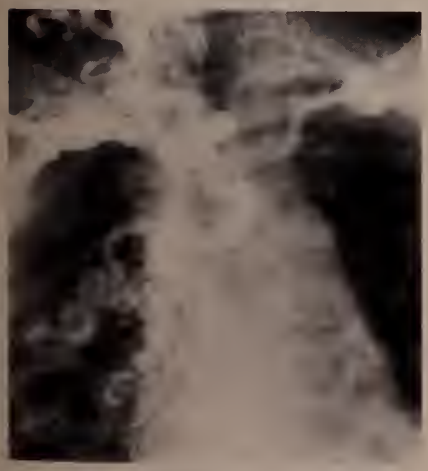

FIGURE 1. Superior vena cavography via bilateral arm injection, performed in Trinidad, reveals tortuosity of superficial chest vessels and of the right subclavian vein, occlusion of the superior vena cava, and filling defects of the right internal jugular and left innominate veins.

In 1963, McLean et al[4] induced hepatic veno-occlusive disease with accompanying pulmonary changes in rats by gastric instillation of a relatively high dose of *Crotalaria* extract. Subsequently, several researchers[5,6] have found that chronic ingestion of low doses of monocrotaline results in pulmonary hypertension in rats, with impaired serotonin transport, medial thickening, pulmonary arteritis, and decreased luminal diameter of the pulmonary arteries in the absence of hepatic toxicity. In certain cases, hypertrophy and chronic inflammation of the right side of the heart were also seen.

In a recent case reported from Great Britain, histologic examination of the pulmonary artery and some of its branches revealed lesions similar to those found in the hepatic venous system.[2] In the patient described here, biopsy of the affected venous vessels demonstrated similar lesions, including medial fibrosis with mural sclerosis and calcification. Pulmonary parenchymal fibrosis was also present.

This patient had extensive disease of the jugular vein, superior vena cava, superior pulmonary vein, mediastinum, and lungs. There was little clinical evidence of liver disease, and a liver biopsy was not performed. The mechanism whereby the lungs became diseased is unclear, but the finding is consistent with experimental work that demonstrates the toxic effects of pyrrolizidine alkaloids on the cardiopulmonary system. If spillover through the liver is postulated, atrial, superior caval, and jugular disease suggests reflux of toxic pyrrolizidines across the atrium into the superior venous system. Localization to the superior pulmonary vein is unexplained. The mechanism does not involve entrapment of major vessels in a process of primary mediastinal fibrosis, but rather is an intraluminal process. This report extends the literature on herbal-tea–induced veno-occlusive disease to include the superior vena cava, innominate vein, and internal jugular vein.

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Thrombocytopenia and fatal intracerebral hemorrhage associated with *Mycoplasma pneumoniae* pneumonia

TO THE EDITOR: *Mycoplasma pneumoniae* is one of the most common causes of respiratory infection in the United States. Manifestations of *M pneumoniae* infection in the respiratory tract are widespread and include pneumonia, sinusitis, otitis media, and tracheobronchitis. Other complications range in severity from myalgias to hemolytic anemia, to aseptic meningitis and meningoencephalitis.[1] Disease due to *M pneumoniae* is generally self-limiting, although treatment with erythromycin or tetracycline may shorten the duration of symptoms.[2]

While morbidity may be extensive, mortality is rare, with fewer than 20 deaths reported in the literature.[3] Even more unusual is significant thrombocytopenia. Recently, we treated a patient who suffered a fatal intracerebral hemorrhage secondary to *M pneumoniae*-induced thrombocytopenia.

Case Report. A 44-year-old man was admitted to the hospital with complaints of cough, numbness in his left hand, and hematuria. He had been well until four days prior to admission, when fever and a cough productive of scanty yellowish sputum developed. He had taken acetaminophen, and his condition had slowly improved. By the morning of admission he was feeling well. However, later in the day, blood in the urine and tingling and numbness of the left hand were noted. His wife observed a change in his behavior and brought him to the emergency room for further evaluation.

There was no history of hematologic disorder or chronic lung disease. No rash or skin lesions had been noted. The patient had taken no other medications and denied drug allergy. He did not smoke cigarettes or drink

alcohol. He had not traveled recently or been exposed to animals.

On examination, he appeared acutely ill and confused. His temperature (taken orally) was 97.5°F; blood pressure, 144/70 mm Hg; respiratory rate, 24/min; and pulse, 120/min. Scattered ecchymoses and petechiae were noted. The conjunctivae were pale, the neck was supple, and heart sounds were normal. Rales were noted at the base of the right lung. An abdominal examination was unremarkable. A rectal examination revealed guaiac positive, burgundy-colored stool. Neurologic examination showed agitation and confusion, but no causative factor could be identified.

Initial laboratory data were notable for a white blood cell count of 20,800/mm^3 with 72% neutrophils, 10% band forms, 3% metamyelocytes, and 1% myelocytes. The hematocrit was 22%, and the platelet count was 7,000/mm^3. The arterial blood gas determination on room air revealed a pH of 7.42; carbon dioxide tension, 39 mm Hg; and oxygen tension, 58 mm Hg. Serum sodium, potassium, and chloride levels were within normal limits. Prothrombin time, activated partial thromboplastin time (APTT), and fibrinogen levels were within the normal range. Acute titers for cold agglutinins were 1:128. Microscopic examination of the urine revealed a full field of red blood cells. Gram's stain of the sputum showed abundant neutrophils and no microorganisms. A peripheral blood smear showed a near absence of platelets, no schistocytes, and no evidence of a microangiopathic process. A chest roentgenogram disclosed an infiltrate in the lower lobe of the right lung.

During the course of the initial evaluation, the patient became apneic and required intubation and mechanical ventilation. The pupils were fixed and dilated. The patient withdrew only from deep pain stimulation.

A computed axial tomographic (CAT) scan of the head revealed a 2 cm hemorrhage in the right brain stem (Fig 1) and obstructive hydrocephalus (Fig 2). Complement fixation titers for *Mycoplasma pneumoniae* were initially 1:8 and, by day 11, had risen to 1:32.

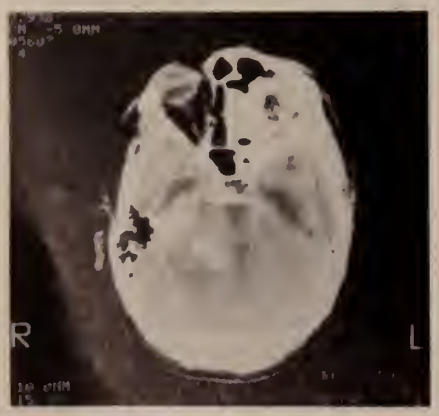

FIGURE 1. CAT scan of the head shows hemorrhagic area in the brain stem.

FIGURE 2. CAT scan of the head shows ventricular dilation and obstructive hydrocephalus distal to the area of hemorrhage.

The patient was maintained on mechanical ventilation. Erythromycin, cefotaxime, amikacin, methylprednisolone, dexamethasone, and cimetidine were administered intravenously. A bone marrow biopsy showed decreased numbers of platelet precursors. Warmed red blood cell and platelet transfusions were administered. Active rectal bleeding ceased, and the platelet count and hematocrit returned to normal over the next few days. The patient's neurologic status remained unchanged. Blood, sputum (routine and mycobacterial), and urine cultures were negative. Serologic tests for *Legionella pneumophila*, influenza A and B, and adenovirus gave negative results. The patient died on the 14th hospital day.

Discussion. The diagnosis of *Mycoplasma* pneumonia is supported by a positive cold agglutinin titer and negative findings on Gram's stain and culture of the sputum. Peak incidence of the disorder is in late fall and early winter. A definitive diagnosis is made either by isolating the organism from the sputum or from throat washings or by demonstrating a four-fold rise in specific complement fixation titers. This patient's complement fixation titers for *Mycoplasma pneumoniae* increased from 1:8 to 1:32 during his 12-day hospital stay, thereby confirming the diagnosis.

Death due to *Mycoplasma* pneumonia is unusual, with fewer than 20 cases reported. The majority of fatalities are due to respiratory complications such as respiratory failure, acute respiratory distress syndrome, or pulmonary fibrosis.[4] Other complications associated with patient mortality include central nervous system involvement with aseptic meningitis or meningoencephalitis,[5] and cardiac involvement with progressive, terminal heart failure.[6]

Hematologic complications are generally limited to hemolysis and/or hemolytic anemia, which is usually associated with elevated cold agglutinin titers.[7] Significant thrombocytopenia is unusual. A search of the literature revealed only two references to this complication. In 1967, Hers and Masurel[8] reported on 83 previously healthy Danish civilians with *Mycoplasma pneumoniae* pneumonia confirmed by serologic tests. Three patients had thrombocytopenic purpura; however, no mention was made of absolute platelet counts, bone marrow studies, or eventual outcome.

Recently, Tsai et al[9] reported on a seven-month-old infant with *Mycoplasma pneumoniae* infection associated with disseminated purpuric lesions and a platelet count of 14,000/mm^3. She responded to minocycline and steroid therapy and was discharged from the hospital with a platelet count of 379,000/mm^3.

We report what we believe to be the first case of fatal hemorrhage secondary to what appears to have been a *M pneumoniae*-induced thrombocytopenia. We speculate that the hemorrhagic tendency was related both to a quantitative decrease in the number of platelets and the abnormal functioning of senescent platelets. The decreased number of megakaryocytes in bone marrow specimens obtained before and after death suggest an immune-mediated destruction of megakaryocyte precursors. The resultant lack of giant megathrombocytes in the peripheral blood smear may explain the increased tendency for hemorrhage as a consequence of metabolic alterations and senescence of the platelet population.

Thrombotic thrombocytopenic purpura (TTP) is not included in the differential diagnosis. TTP is characterized by normal to increased peripheral destruction of platelets, and this was not the case here. In addition, postmortem samples of spleen, lymph node, bone marrow, and small vessels showed no deposition of collagen or microthrombi suggestive of TTP.

Disseminated intravascular coagulation from overwhelming infection can lead to thrombocytopenia. However, prothrombin time, APTT, and fibrinogen levels were all within normal limits, thereby excluding this diagnosis from consideration.

Mycoplasma pneumonia is usually, but not always, a benign disease. Outpatient therapy with either erythromycin or tetracycline will suffice in the typical case. However, if there is evidence of a bleeding disorder or thrombocytopenia, early admission to the

hospital is advised. Aggressive attempts at hemostasis, in addition to antimicrobial therapy, should be implemented.

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FROM THE LIBRARY

POLYCYTHEMIA VERA

Report of Ten Cases Treated With Phenylhydrazine

Polycythemia vera (Erythremia, Splenomegalic polycythemia, Vaquez's Disease, Osler's disease), is a chronic disease characterized by an increase in the number of the red blood cells. The spleen is usually enlarged, sometimes tremendously. Minot says the disease is a new growth of the red blood cells.

The etiology is unknown. The onset is extremely gradual, and the condition may go unnoted for years. There is no known cure, but the progress of the disease is so slow that death is often due to other causes. Patients frequently reach an advanced age. They are poor surgical risks and have but little resistance to any infection.

In 1918 Eppinger and Kloss first treated erythremia with phenylhydrazine. Seven years later, in this country, Owen followed their example and was enthusiastic about his results. Brown and Giffin, Altnow and Carey, Stealy and Cabot were among those to report cases benefited by the drug. In 1927 Bryan reported unsatisfactory results in one case and two years later Giffin and Conner called attention to the danger of giving the drug to those who were bed-ridden; over 60 years old, who suffered from arteriosclerosis or gave "evidence of advanced visceral injury."

McNamara and Sansum reported a case of poisoning from phenylhydrazine in a woman who had been given large doses by an osteopath. This case is particularly interesting because in all probability the patient did not have the disease.

Harrop's article is a very comprehensive survey of the whole subject of polycythemia. He discusses the effect of the drug, but does not think there is any definite proof that a normal liver is injured by its continuous use. Owen feared this, as have other observers. Cirrhosis is of course a not unusual complication of erythremia.

In treating such a slowly progressing disease as this, is it justifiable to use such a dangerous drug? Is the benefit sufficient and improvement enduring enough to warrant the risk? After studying ten cases in the Presbyterian Hospital and Vanderbilt Clinic, we think that the drug is indicated and to some patients may offer at least as much as any other form of therapy. . . .

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(*NY State J Med* 1933, 33:1039-1045)

AIDS: ETIOLOGY, DIAGNOSIS, TREATMENT AND PREVENTION

Edited by Vincent T. DeVita, Jr, MD, Samuel Hellman, MD, and Steven A. Rosenberg, MD. 352 pp, illustrated. Philadelphia, JB Lippincott Co, 1985. $39.75 (hardcover)

One of the hobbies of those involved in the care and treatment of patients with acquired immunodeficiency syndrome (AIDS) is examining new texts on this subject to determine how out of date they are. In this rapidly moving field, published articles become rapidly obsolete; consequently, the delay involved in assembling and publishing a text on AIDS makes it a risky enterprise. However, even though *AIDS: Etiology, Diagnosis, Treatment and Prevention* contains some outdated information, the benefits of this text far outweigh the disadvantages.

The first part of this book deals with the epidemiology of AIDS and presents a detailed discussion of recent developments. The immunology and the pathology of AIDS and the AIDS-related complex (ARC) are discussed. Several chapters are devoted to the clinical findings in AIDS patients, specifically the infectious and neoplastic complications of the disease. Finally, the psychosocial aspects of AIDS are discussed, as well as safety precautions involved in the care of AIDS patients.

This text was edited by three well-known researchers who are or have been associated with the National Cancer Institute. Although they themselves have had limited clinical and research experience with AIDS, they have assembled a group of contributors from the National Institutes of Health (NIH) that have extensive experience in both research and patient care. The chapter on the etiology of AIDS is co-authored by Robert Gallo, the virologist who isolated HTLV-III at the NIH. Donald Abrams of San Francisco General Hospital has co-authored a lucid chapter on the AIDS-related complex. Anthony Fauci, an immunologist who has done much to characterize the alteration in the immune system, describes the immunologic features of AIDS. All the chapters are well referenced, and the book has a number of black-and-white and color plates depicting the pathologic features of the disease.

This book brings together many of the issues related to AIDS that have previously been discussed in either the medical literature or at conferences. The chapters are written in a clear and concise manner. Several summary sections describe prospects for diagnostic tests, therapy, and future avenues of research on the virus that causes AIDS.

This book will provide a useful addition to the library of the clinician who sees patients with AIDS or those persons at risk. In addition, physicians will find it helpful in reviewing the issues necessary to answer patients' questions about the disease. Finally, those institutions that are beginning to confront this disease will find it a useful resource for developing staff education programs and protocols to protect personnel and patients.

In short, if there is one text to recommend on this subject, this is the one. Although progress on this disease will make this book obsolete earlier than most medical books, many practitioners will find this text useful now.

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THE MANAGEMENT OF AIDS PATIENTS

Edited by David Miller, Jonathan Weber, and John Green. 202 pp, illustrated. Dobbs Ferry, NY, Sheridan House, Inc, 1986. $24.50 (paperback)

An American physician might initially be disinclined to view this book as useful for three reasons. First, it was written by British clinicians at St Mary's Hospital in London. Second, compared to the far more extensive epidemic in the United States, the authors' experience is limited to fewer than 700 patients with HTLV-III infections, almost all of whom are homosexual men. And third, because of the rapid advances in the understanding of AIDS-related disorders, a book written a year ago is bound to be outdated.

These initial reservations, however, are dispelled once one reads this excellent text in more depth and finds that the above three disadvantages are actually advantages. First, the British orientation serves as a reminder that AIDS is an international problem and that the medical and psychosocial issues can be generalized. Second, the relatively small number of patients has permitted an in-depth exploration and a willingness to cite the literature where personal experience is limited. And third, although no text can possibly incorporate each new published finding, it is valuable to have a cogent and articulate scaffolding on which to add current and future advances. In fact, the reader will soon discover that these advances do not, in general, contradict past views (mid-1985) but rather supplement them.

But by far the greatest value of this book is its emphasis on the practical. By this I do not mean to suggest that it merely outlines "cookbook" recommendations without sufficient emphasis on the scientific rationale and complexities of clinical care. On the contrary, the virology, epidemiology, and immunology of HTLV-III infections are clearly explained even for those not especially knowledgeable in these areas. Rather, by "practical" I mean that the chapters deal with what practicing clinicians need to know when confronted with an AIDS-related disorder. For example, the authors present the expected course of the disease and describe how one makes the diagnosis (complete with a description of common physical findings; recommended laboratory tests; photographs depicting oral candidiasis, leukoplakia, and Kaposi's sarcoma; and an x-ray showing pneumocystis pneumonia, etc); how one treats an opportunistic infection of the gastrointestinal tract, lung, or central nervous system; how one specifically counsels patients with hemophilia, individuals with seropositivity, and concerned family members about "safe sex" and other risk-reducing procedures; infection precautions necessary for nursing care and disposition of the body after death; and interventions helpful for the worried well.

Given the relative newness of the AIDS epidemic and the absence at present of an effective cure or vaccine, clinicians may tend to feel frustrated and helpless. This is the very book to allay those feelings and indicate that one need not be an "AIDS expert" to help these patients. There is much we have to offer in terms of an accurate diagno-

sis, palliative care, counseling, and education—tasks that are familiar to all clinicians.

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AIDS AND THE EMPLOYER. GUIDELINES ON THE MANAGEMENT OF AIDS IN THE WORKPLACE

Edited by Leon J. Warshaw, MD. 86 pp. New York, The New York Business Group on Health, Inc, 1985. $30.00 (softcover)

Although the social and medical issues that AIDS presents are well publicized, this epidemic has created unique problems for employers. In addition to employee concerns about contact with coworkers with HTLV-III–related diseases, AIDS-related problems have emerged in such areas as modification of benefit plans, cost impact of the disease, and hiring or placement procedures for employees who are seropositive for the AIDS virus.

This publication presents the proceedings of a New York Business Group on Health (NYBGH) forum on "AIDS and the Employer" that was held in December 1985. The goals of the forum were to alert employers to the importance of AIDS in the workplace and to discuss the options available in dealing with the problems that this disease presents.

The first section of the book presents an overview that addresses four key issues: the potential impact on employers, the medical background, the health and support systems needed by persons with AIDS, and the legal and regulatory constraints that currently exist. This is followed by the presentation of 13 hypothetical cases and comments by a panel with broad experience in the field of health care issues in the workplace. The appendix includes a compendium of educational material and resources available on AIDS, as well as sample company policies and employee communications on the disease.

Dr Warshaw, the editor, has succeeded in assembling a worthy group of contributors with broad experience in the legal, social, and medical aspects of health problems in the occupational setting. Although all publications on AIDS run the risk of being outdated prior to publication, the information is presented here within the framework of dealing with day-to-day issues that will continue to confront employers. Consequently, although details may change, principles will not. In this respect, the case presentation section is the book's most valuable asset.

This volume will be most useful for small organizations and/or their consultants who are beginning to face the problems AIDS presents in the workplace. Larger employers will probably be able to take advantage of legal and medical resources that already have experience with the issues that accompany this disease.

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CLINICAL PRACTICE AND COST CONTAINMENT. A PHYSICIAN'S PERSPECTIVE

By Henry A. Shenkin, MD. 144 pp. Westport, Conn, Praeger Publishers, 1986. $39.95 (hardcover)

> Now that it is evident that runaway costs have finally broken the back of resistance to fundamental change in the funding of our health care system it will soon be clear that the changes will be monumental, including their effect on physicians.
>
> —Henry A. Shenkin, MD

Henry A. Shenkin, MD, practiced neurosurgery from 1945 to 1982. During these 37 clinical years, he published 138 scientific papers.

Truly the angels must rejoice when a practicing physician with impeccable clinical credentials and professional experience shifts the focus of his attention from the mundane concerns of clinical practice to the broader issues of health care delivery, community health planning, health care funding, and the other subjects that constitute an up-to-date curriculum in health administration.

Within the 144 pages of this book, Shenkin manages to include for discussion a fair representation of the contemporary dilemmas that bedevil attempts at cost containment within clinical practice.

Shenkin writes:

> This book, it is hoped, will fill the hiatus in knowledge about the problems of the cost of medical care and how remarkable the changes are in progress. The facts leading to these changes and their effect on doctors' practices and status should be of particular interest to young physicians, residents, and medical students. Perhaps with an understanding of the reasons for the present turbulence in our health delivery systems they will be able to choose better what role they and their organizations should play in obtaining their most desired goals.

Somewhat intuitively, the current 10.5% of the gross national product (GNP) is deemed the appropriate percentage that is justifiable to spend on health care in its varieties of manifestations. To spend a larger percentage than 10.5% is to risk ignoring completely high priority budgetary items with their own legitimate claims.

Money is being misspent to pay for the costly high technology of tertiary care, whereas the imperatives of frugality would dictate preventive medicine programs as preferable.

The present-day physician glut, growing ever larger, has weakened the power of physicians and has placed hospitals in powerful bargaining positions vis-a-vis expenditures in health services. One example: hospitals are now hiring radiologists and pathologists and placing them on hospital payrolls as salaried employees. In the past, the advent of Medicare facilitated the hard bargaining of hospital radiologists and pathologists who demanded and obtained astronomical fees for services as independent practitioners.

Shenkin reminds those hostile critics who would righteously deplore the self-serving economic maneuvering of physicians that physicians as a categorical group are not unique in their efforts to maximize their incomes. Rather than condemnation, Shenkin argues for a sophisticated analytic approach in order to identify and deal with the etiologies of such behavior. A total systemic change is called for—one that would tap the economic motivations of physicians. To promote improved social behavior, he advocates competition among hospitals. He would rely on the pressures of the marketplace to promote efficiency.

Resources are finite. Objectives in health care are infinite. To reconcile the two, prioritization is necessary. This means that rationing of services is necessary. Given this scenario, ethical problems are inevitable.

Shenkin reviews the spotty record of attempts over the years to contain costs. He focuses on the health care systems in the United Kingdom and Canada, countries that are culturally similar to the United States.

He supports the concept of a national health system. He recognizes that in the

present sociopolitical climate there is little chance of implementing such a break with American tradition. However, in Shenkin's view the development of a national health system is inevitable. He advises physicians to become involved as early as possible so as to have some significant say in crafting such a national health system. If physicians remain aloof, corporate managers and hospital administrators will inexorably displace physicians from strategic positions of decision-making and political power.

The book contains a useful albeit introductory collection of topics for medical students and hospital house officers. The book is less useful for administrative health professionals who are up to date and who will insist on greater depth in the analyses. The small size of the book represents the ultimate limitation of such an in-depth discussion.

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ANESTHESIA FOR THE UNINTERESTED

Second Edition. By John D. Tolmie, MD, and Alexander A. Birch, MD. 263 pp, illustrated. Rockville, Md, Aspen Publishers Inc, 1986. $19.96 (paperback)

This book is intended to be an introductory text for students rotating on an anesthesia service. As such, it serves as an adjunct to the anesthesiologist faced with the difficult task of convincing students that anesthesia is more than "long periods of boredom interrupted by moments of terror."

The editors have assembled an impressive array of authors to write the 29 chapters in this book and they cover a great deal of material. The book is divided into six sections encompassing a very brief history of anesthesia, pre-operative evaluation of the patient, preparation of anesthetic equipment, anesthetic administration, anesthetic subspecialties, and the anesthesiologist's role outside the operating room.

The book is easy reading and can no doubt "be painlessly consumed in a few evenings" as suggested in the preface by the editors. One could argue about the precise accuracy of some of the material presented here, but the book is not intended to be a definitive reference source. In fact, the authors have done an admirable job of presenting enough information to keep uninterested students interested without overwhelming them. The book is very well indexed but the chapter references are very outdated. The glossary, on the other hand, is very good and quite amusing.

There are better books available to students who desire a more comprehensive overview of anesthesia. *Understanding Anesthesia* by Robert M. Julien and *Anesthesiology: A Manual for Medical Students* by Rhonda D. Levine are two such examples. However, as the title suggests, the book under review does not pretend to be geared for such students.

The book, particularly the illustrations, is somewhat light-hearted in its approach and this certainly helps make it so readable. However, I fear that not all readers will appreciate the numerous illustrations featuring attractive, scantily clad women.

The editors aptly describe anesthesia as a discipline encompassing the whole spectrum of medicine. On balance, this book, in combination with an enthusiastic preceptor, will go a long way in helping students appreciate that description.

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TUMOR MARKERS: CLINICAL AND LABORATORY STUDIES

By Janis V. Klavins, MD. 214 pp, illustrated. New York, Alan R. Liss, Inc, 1985. $48.00 (hardcover)

This book tries to organize the extensive field of tumor markers into an accessible, understandable form for the clinician, the investigator, and the student.

In the first chapter, the author groups the markers in the categories of oncofetal gene products, tumor-associated markers, and tumor-specific markers; a system that she had discussed in a previous paper. These categories are further subdivided into markers with universal distribution, those appearing in embryonic tissue and in malignant tumors derived from all three germinal layers, and those with limited distribution, appearing in only a few malignant or normal cell lines. With the rapid expansion of the field, it is understood that markers so designated may shift position among the categories as new information appears.

In subsequent chapters, the markers are listed under the headings of the various malignancies. For breast cancer, we find five oncofetal markers, 12 tumor-associated markers, and five tumor-specific markers. The discussion of each marker is brief, almost in abstract form, but does provide a quick survey of the established substances as well as some newly defined ones that are thought to be relevant for diagnosis and monitoring of each malignancy. The reference list is extensive, including several works by the author herself.

The author seems at ease with the biochemical and clinical aspects of the field and the plan of presentation is a good one, but the text is difficult reading and organizational problems make comprehension a bit of a struggle. Sentences are heavy with data and references. At times, paragraph cohesion is poor. Discussion of a work begun in one paragraph may run over into part of the next. Discussion of several other markers may wander into the comments on the cited marker. The plan to organize the markers into the three major groups under each specific malignancy is not always carried out. The type used for headings and subheadings is not consistent throughout the book, thus causing the reader to lose a sense of the relationships among the substances. Two hand-drawn diagrams attempt to compare the appearance of normal differentiated and undifferentiated cells to that of tumor cells. Pictures of actual cells would be more telling. There is little mention of the molecular biology that underlies this field of research. Users of the book will be compelled to search out the references to evaluate the presented data.

For the clinician, the book can serve as a reference catalog of markers that relate to a given malignancy, but most of the markers are research tools and not practical for day-to-day work. The investigator can gather a base of reference information from which new programs of research can be elaborated. The student may use the book as a guide to the literature but will need to fall back on previous knowledge of genes, cell membrane structure, and tumor biology to put the data into place.

Overall, the book performs best as a reference work, an extensive annotated bibliography of the current status of tumor markers.

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THIRTY-FIVE YEARS IN THE TOWER

By Solomon Papper, MD. 155 pp. Boston, Little, Brown and Co, 1985. $19.95 (hardcover)

When asked to review this book I accepted immediately. Dr Papper and I became acquainted during the years he served as a Governor of the American College of Physicians representing Oklahoma. He impressed me then as a humane and dedicated clinician and teacher. Reading his book confirms that impression. In the first chapter he lists a "Cast of Characters" and accurately and amusingly describes each one. Included are The Basic Science Faculty, The Clinical Faculty, Administrators, Teacher Types, The House Staff, Secretaries, and The Licensed Bureaucrats. Medical Educators and Voluntary Faculty will readily recognize them and recall individuals to fit each category from their own experiences. The author expertly blends truth and humor; that makes his work delightful and easy to read. His portrayal of medical school committees brought a smile to my face. Under the subheading of Nonaccomplishment, Papper explains the four devices used to achieve that laudable result: the nonaccomplishment approach, the dilutional approach, the direct approach, and the democratic approach.

Dr Papper mocks recruitment procedures and search committees. The words are funny but the implications are sad. Papper also writes about managers versus leaders, the intimidation of faculty, student hypocrites, dehumanization, the house staff in action, and the power structure. I found myself involuntarily nodding in agreement.

In the fifth chapter a fictitious contract is depicted. It ends with 11 lines for signatures, one each for the administrator and his associate, seven for assistant administrators, one for a chairman, and the last for the dean. Patient care is covered in eight and one half pages and the comments are right on target.

Obviously, I enjoyed this book. It is full of good common sense and humor. Our medical schools could use many like Dr Papper. I recommend this book to all who participate in medical education, especially full-time faculty members, house officers, and students.

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YOUR PERSONALIZED HEALTH PROFILE: CHOOSING THE DIET THAT'S RIGHT FOR YOU

By Myron Winick, MD. 263 pp, illustrated. New York, William Morrow and Co, 1985. $16.95 (clothcover)

Dr Winick has written a layman's guide to nutrition that allows readers to decide whether they are at high, moderate, or low risk for one or more of seven serious, nutrition-related diseases. The book also provides guidelines for appropriate dietary modifications. By acquiring information about the diseases—atherosclerosis, hypertension, obesity, cancer, diabetes, anemia, and osteoporosis—and his or her personal risk profile, the individual bears the burden for making changes, rather than relying on group intervention. The knowledge base emphasizes family history and provides information about values of specific risk factors such as blood pressure and blood lipids.

Dr Winick is eminently qualified to write such a guide. He has been in the forefront of American academic medical nutrition for many years and his investigations have greatly contributed to scientific knowledge, especially in the areas of maternal and infant nutrition and diet and behavior. This book provides factual, practical, and sound information on important and popular topics that should offset some of the faddish information, often bordering on outright quackery, that is regularly published. Thus, the physician can suggest this volume to his patient and be confident about the source and accuracy of the information provided. The format is such that as new information breaks it may be incorporated within the framework of the chapters. Within each topic the 16- to 37-page chapters introduce the disease with a relatively nontechnical description, discuss the advantages and disadvantages of possible choices, and include menu planning. Much of the material is presented in tables.

Presumably another clinical nutritionist might have chosen a slightly different set of data with varying emphasis, but those differences would not necessarily have made for a better book. There are a few editing flaws that merit correction. On page 187, in Chapter 7 on Anemia, the adult woman's zinc requirement is stated as 5 mg with 10 mg/d "more than adequate." In fact, the zinc requirement is 15 mg/d. On the same page a supply of folic acid of 5 mg is deemed adequate; here it is not clear what amount was meant for the woman at risk. For some unexplained reason, Tables 1, 2, 11, 12, 14, and 15 lack headings; Tables 17 and 25 in Chapters 6 and 10, respectively, are identical representations of the fiber content of 40 common foods. On page 244, the reference to Table 23 should state Table 25. Incidentally, it was not always clear to me whether part scores could be used for some risk factors as I tried to calculate my profiles.

The overall organization and style of the book make it easy to follow. The author's recommendations incorporate the reader/patient's intelligence, concern, and curiosity regarding health, disease, and diet. Where appropriate, patients are referred to their physicians for further guidance. While this nutrition publication falls into the category of "self-help" books, it does not sermonize or make outrageous promises. Rather, it provides a sound and sensible approach to improving health through accurate, personalized nutrition knowledge with which one takes action.

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New name proposed for the AIDS virus

The group of viruses believed to cause acquired immunodeficiency syndrome (AIDS) is referred to by a variety of names. This has created considerable confusion in the medical literature, the lay press, and at scientific meetings. A nomenclature committee of the International Committee on the Taxonomy of Viruses has proposed the name human immunodeficiency virus (HIV) for the AIDS virus.

The virus found to cause AIDS was originally given different names by its discoverers on either side of the Atlantic. At the Pasteur Institute in Paris, the name given was lymphadenopathy-associated virus (LAV); human T-lymphotropic virus type III (HTLV-III) was the name decided on at the National Cancer Institute. As part of the continuing controversy over which research team first discovered the virus, each faction has lobbied for the use of either LAV or HTLV-III. Many scientists and editors have avoided taking sides in this debate by calling the AIDS virus HTLV-III/LAV. Other names to arise later from laboratories that isolated the virus include AIDS-associated retrovirus (ARV) and immunodeficiency-associated virus (IDAV).

Eleven of the 13 members of the nomenclature committee signed a letter published in *Science* (1986; 232:697) proposing worldwide acceptance of the designation HIV. The authors of the letter chose the name based on the following criteria: "the name conforms to common nomenclature for retroviruses, beginning with the host species ('human'), ending with 'virus,' and containing a word that denotes a major (though not the only) pathogenetic property of the prototypic members of the group ('immunodeficiency')"; HIV does not mention AIDS—the name associates the virus with the disease, but infection with HIV does not necessarily imply a disease state; and the name is in no way related to "priority of discovery."

The committee suggested that individual laboratories develop a code of letters and numbers—indicating the geographic site and the sequence of discovery—to identify their isolates.

Variant of AIDS virus may protect against the disease

A new variant of the AIDS virus was discovered this year by a research team from the Harvard School of Public Health in Boston. As reported in *Science News* (1986; 129(14):212), the researchers first identified the virus, called HTLV-IV, in healthy prostitutes in Senegal. The virus is very similar to HTLV-III/LAV—the "AIDS virus"—based on their mechanisms of action and antibody cross reactivity.

The astonishing finding, based on studies of more than 50 Senegalese infected with HTLV-IV, was that this population seemed to stay healthy. Despite the presence of AIDS in neighboring countries, there has been only one reported case of AIDS in Senegal; and the research team found no signs of asymptomatic infection with HTLV-III/LAV.

These findings suggest that infection with HTLV-IV could serve as a natural form of protection against AIDS—an intriguing model for the development of an AIDS vaccine.

Keeping the nation's blood supply safe

Blood banks nationwide have achieved much success in screening donor blood for human immunodeficiency virus (HIV)—the virus shown to cause AIDS. There is, however, still some risk of HIV-infected blood escaping detection using current ELISA tests. An evaluation of available testing procedures and those under development was part of the agenda addressed by the panel at a recent National Institutes of Health Consensus Development Conference.

The risk of false negative test results in the early stages of infection—antibody levels may be too low to detect weeks or even months after a donor is exposed to the AIDS virus—was noted in the American Association of Blood Banks' publication *News Briefs*. Panel members commented on the variable sensitivity levels among ELISA tests from different manufacturers and the possible benefits of performing multiple tests on a single sample.

The panel expressed hope for even more accurate blood testing in the future, with the development of fluorescence assays to detect infected T lymphocytes and improved techniques for identifying viral proteins.

Five-year projections for AIDS

The United States Public Health Service foresees a greater than ten-fold increase in the incidence of AIDS during the next five years. The government agency estimates that by 1991 there will have been 54,000 deaths in the US attributable to AIDS. In comparison, AIDS has been reported in 21,000 persons in the US and has accounted for 11,000 deaths during the past five years. The cumulative death toll could reach 179,000 by 1991.

Health care costs for treating patients with AIDS and associated disorders could soar to $16 billion a year. Public Health Service forecasters do not anticipate an effective immunization program for persons at high risk of contracting AIDS for up to ten years.

NEWS BRIEFS are compiled and written by Vicki Glaser.

Physicians testify for medical liability reform

In August, Dr John Finkbeiner, president of the Medical Society of the State of New York (MSSNY), and Dr Linda Robinson, chairman of the Commission on Membership and Member Services of the New York State Academy of Family Physicians, presented testimony to the House of Representatives Judiciary Subcommittee on Administrative Law. The subcommittee is considering HR 2659, the Medical Malpractice Reform Act, which was introduced by Congressman Robert Mrazek of New York. Following is a synopsis of the testimony presented by Drs Finkbeiner and Robinson.

For more than ten years, physicians in New York State have faced almost yearly increases in medical liability insurance premiums. And, since 1984, these increases have been assessed on a retroactive basis. Rising insurance costs in New York State are forcing many doctors to change the way they practice medicine, to move their practices to other states, or to abandon the medical profession. "This year for the first time in my professional life, I can report to you that the available residency positions in New York State in obstetrics and gynecology are not being filled," noted Dr Finkbeiner. "Students . . . are leaving New York in unprecedented numbers after their educations have been completed."

Although legislation to combat this problem has been adopted in various states, the medical liability crisis affects the entire nation and requires action on the part of the federal government. "HR 2659 introduced by Congressman Robert J. Mrazek of New York embodies a most thoughtful and promising approach to resolving this problem at the federal level," according to Dr Finkbeiner.

In 1985 and 1986, the New York State legislature enacted laws aimed at controlling spiraling insurance costs. Dr Finkbeiner applauded these initial efforts and presented several key features of the legislation, including the reduction of contingency fees and greater sanctions to discourage frivolous lawsuits. The 1985 law determined that awards of future damages could be paid in the future, rather than upon settlement of the suit. (It has been estimated that this action alone could reduce malpractice system costs in New York State by approximately 18%.) In addition, the law introduced a program in which hospitals would provide physicians with supplemental insurance coverage of $1 million per incident and $3 million per year, at no direct cost.

But Dr Finkbeiner insisted that further legislation is needed. He outlined the three provisions deemed by MSSNY to be essential for effective medical liability reform: "a limit of $250,000 on awards of non-economic damages"; "a limit on the personal liability of physicians in malpractice cases to the limits of liability insurance presently available for purchase directly by physicians in New York, which is $1 million per incident and $3 million per year"; "a rollback of premiums to the level in effect on June 30, 1984."

Finally, Dr Finkbeiner urged the representatives to follow New York State's lead in "encouraging arbitration as an alternative to the jury system." HR 2659 provides for the establishment of medical malpractice arbitration panels which would adjudicate and set awards in all malpractice suits. "Too many medical liability cases are decided on the basis of maloccurrence rather than malpractice," stated Dr Finkbeiner. "The Medical Society of the State of New York supports the proposed legislation HR 2659," he concluded. "The bill promises substantive change in an area where such change has been long past due."

Dr Robinson, a family physician from upstate New York, described the detrimental effects that the medical liability insurance crisis is having on family physicians, especially those in inner city and rural regions. "The medical malpractice situation affects family physicians in special ways owing to the nature of the primary care relationship and the style of medicine practiced," according to Dr Robinson. "The present and future status of the specialty may be at risk if the liability problem is not satisfactorily resolved."

Dr Robinson presented the results of a survey conducted by the New York State Academy of Family Physicians, in which members reported actions they are taking to cope with the increases in medical liability premiums. The results to date are as follows: 2.9% of respondents have left private practice; 7.9% have reduced their practices from full-time to part-time; 4.0% are considering early retirement; 40% are accepting fewer or no new Medicaid patients; 35% have reduced the amount of charity care they provide; and 27% of those who offer obstetrical care will no longer practice obstetrics. In addition, 61% of respondents have increased referrals and 68% are performing more diagnostic tests, indicating a shift toward more defensive medicine in order to avoid litigation.

The malpractice crisis is crippling the medical profession and threatens the availability of quality health care. Lawsuits erode the trusting relationship between patient and physician. And increasing liability premiums often result in increased fees, thus preventing persons with low or fixed incomes from obtaining adequate medical services.

"Family physicians are hoping for a solution to this malpractice problem," observed Dr Robinson. "They would like to regain the trust of their patients, to accept all those in need of medical treatment without financial discrimination, and find young physicians to join them in practice."

MEDICAL SOCIETY NEWS is written by Vicki Glaser.

OBITUARIES

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Jules Bryan Aaron, MD, Lighthouse Point, Florida. Died August 20, 1986; age 72. Dr Aaron was a 1939 graduate of State University of New York Downstate Medical Center. He was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the American Society of Internal Medicine, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Hernan Roberto Aguilar, MD, Jackson Heights. Died April 11, 1986; age 36. Dr Aguilar was a 1936 graduate of Facultad de Ciencias Medicina de la Universidad de Buenos Aires. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Harry Benjamin, MD, New York. Died August 24, 1986; age 101. Dr Benjamin was a 1912 graduate of Eberhard-Karls-Universität Medizinische Fakultat, Tübingen, Wurttemberg. He was a member of the American Geriatrics Society, the New York County Medical Society, and the Medical Society of the State of New York.

Harry J. Bettauer, MD, New York. Died July 3, 1986; age 84. Dr Bettauer was a 1927 graduate of Medizinische Fakultät Universität Heidelberg, Heidelberg. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Herbert Richard Blain, MD, White Plains. Died August 8, 1986; age 80. He was a 1932 graduate of the University of Edinburgh Faculty of Medicine. Dr Blain was a member of the American Rheumatism Association, the New York County Medical Society, and the Medical Society of the State of New York.

Stephen J. Bruno, MD, Flushing. Died June 27, 1986; age 70. He was a 1943 graduate of Laval University Faculty of Medicine, Quebec. Dr Bruno was a Qualified Fellow of the International College of Surgeons and a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Robert B. Burtch, MD, Alexandria Bay. Died April 1, 1986; age 68. Dr Burtch was a 1943 graduate of State University of New York Upstate Medical Center, Syracuse. He was a Fellow of the American Academy of Family Practice and a Diplomate of the American Board of Family Practice. His memberships included the American Geriatrics Society, the Medical Society of the County of Jefferson, and the Medical Society of the State of New York.

John Mario Cammarata, MD, Bronxville. Died August 23, 1986; age 69. He was a 1947 graduate of the College of Physicians and Surgeons, Boston. Dr Cammarata was a member of the Academy of Medicine, the Radiological Society of New York State, the Radiological Society of North America, Inc, the Society of Nuclear Medicine, the Bronx County Medical Society, and the Medical Society of the State of New York.

Edward J. Carey, MD, Cooperstown. Died June 30, 1986; age 52. He was a 1958 graduate of Cornell University Medical College, New York. Dr Carey was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Orthopedic Surgery. His memberships included the American Academy of Orthopaedic Surgeons, the Medical Society of the County of Otsego, and the Medical Society of the State of New York.

Sylvester J. Carter, MD, New York. Died July 24, 1986; age 78. He was a 1939 graduate of Boston University School of Medicine. Dr Carter was a Fellow of the American College of Surgeons and a Qualified Fellow of the International College of Surgeons. He was a member of the Academy of Medicine, the Pan American Medical Association, the American Society for Surgery of the Hand, the New York County Medical Society, and the Medical Society of the State of New York.

Benjamin Victor DiIorio, MD, Utica. Died August 13, 1986; age 84. Dr DiIorio was a 1930 graduate of Cornell University Medical College, New York. He was a Fellow of the American College of Anesthesiologists and a Diplomate of the American Board of Anesthesiology. His memberships included the Academy of Medicine, the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

Joseph DiMaio, MD, North Tarrytown. Died June 19, 1986; age 80. Dr DiMaio was a graduate of Facoltà di Medicina e Chirurgia dell'Università di Napoli. He was a Fellow of the American College of Anesthesiologists and a member of the New York State Society of Anesthesiologists, the American Society of Anesthesiologists, Inc, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Richard D. Dugan, MD, Tappan. Died July 16, 1986; age 60. He was a 1953 graduate of New York Medical College, Flower and Fifth Avenue Hospitals. Dr Dugan was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the Medical Society of the County of Rockland and the Medical Society of the State of New York.

Samuel Feldman, MD, Ossining. Died July 12, 1986; age 55. Dr Feldman was a 1959 graduate of Faculté de Médicine de l'Université de Lausanne. He was a member of the Academy of Medicine, the American Psychiatric Association, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Arthur Forst, MD, Delray Beach, Florida. Died July 29, 1986; age 77. He was a 1938 graduate of George Washington University School of Medicine, Washington, DC. Dr Forst was a member of the American Geriatrics Society, the American Academy of Family Practice, the Medical Society of the County of Rockland, and the Medical Society of the State of New York.

Maria Z. Fuchs, MD, New York. Died July 31, 1986; age 81. Dr Fuchs was a 1935 graduate of Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia. She was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychiatric Association, the Academy of Psychoanalysis, the New York County Medical Society, and the Medical Society of the State of New York.

Leo Arthur Fox, MD, Scarsdale. Died June 18, 1986; age 80. He was a 1932 graduate of State University of New York Downstate Medical Center. Dr Fox was a member of the American Academy of Family Practice, the Bronx County Medical Society, and the Medical Society of the State of New York.

Julius Peter Gale, MD, Lindenhurst. Died July 4, 1986; age 80. Dr Gale was a 1932 graduate of Columbia University College of Physicians and Surgeons. He was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Joseph L. Gottesman, MD, Great Neck. Died March 10, 1986; age 82. He was a 1927 graduate of Tufts University School of Medicine, Boston. Dr Gottesman was a member of the International Academy of Proctology, the American Academy of Family Practice, the Academy of Psychosomatic Medicine, the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Charles Greenberg, MD, Nyack. Died July 21, 1986; age 80. He was a 1932 graduate of Rush Medical College, Chicago. Dr Greenberg was a Fellow of the American Psychiatric Association, a Diplomate of the American Board of Psychiatry and Neurology, and a member of the Academy of Medicine, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

Martin H. Greenfield, MD, Boca Raton, Florida. Died April 3, 1986; age 87. Dr Greenfield was a 1927 graduate of the Medical College of Virginia, Richmond. He was a member of the American Academy of Family Practice, the American Society of Clinical Hypnosis, the Pan American Medical Association, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Albert J. Griesbach, MD, Laguna Hills, California. Died July 8, 1986; age 92. Dr Griesbach was a 1920 graduate of Medizinische Fakultät-Georg-August Universität Göttingen, Niedersachen. He was a member of the Medical Society of the County of Queens and the Medical Society of the State of New York.

Virginia I. Haggerty, MD, Brooklyn. Died July 19, 1986; age 60. She was a 1951 graduate of New York University College of Medicine. Dr Haggerty was a Diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Edward Emanuel Harkavy, MD, New York. Died July 25, 1986; age 84. He was a 1927 graduate of Yale University School of Medicine, New Haven. Dr Harkavy was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychoanalytic Association, the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

Herman Hirschfeld, MD, New York. Died August 6, 1986; age 82. Dr Hirschfeld was a 1935 graduate of University of Oklahoma School of Medicine, Oklahoma City. He was a member of the American Academy of Compensation Medicine, Inc, the American Occupational Medical Association, the American Geriatrics Society, the American Academy of Dermatology, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Sydney Leider, MD, New York. Died August 13, 1986; age 72. Dr Leider was a 1938 graduate of New York University College of Medicine, New York. Dr Leider was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Surgery, and a member of the Academy of Medicine, the New York County Medical Society, and the Medical Society of the State of New York.

John Anthony Leone, MD, Lewiston. Died July 12, 1986; age 83. Dr Leone was a 1927 graduate of the University of Buffalo School of Medicine. He was a Fellow of the American Academy of Family Practice and a member of the Academy of Medicine, the Medical Society of the County of Niagara, and the Medical Society of the State of New York.

Robert B. Lerrick, MD, Yorktown Heights. Died July 10, 1986; age 61. He was a 1947 graduate of New York University College of Medicine. Dr Lerrick was a Fellow of the American College of Allergists and a Diplomate of the American Board of Pediatrics and the American Board of Allergy and Immunology. His memberships included the Academy of Medicine, the American Academy of Pediatrics, the American Academy of Allergy, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Gustav Machol, MD, Brooklyn. Died July 24, 1986; age 83. He was a 1926 graduate of Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia. Dr Machol was a member of the American Psychiatric Association, the American Board of Legal Medicine, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Charles Theodore Mann, MD, Lockport. Died July 2, 1986; age 71. Dr Mann was a 1941 graduate of the University of Rochester School of Medicine and Dentistry. He was a Diplomate of the American Board of Anesthesiology and a member of the Academy of Medicine, the Pan American Medical Association, the Medical Society of the County of Niagara, and the Medical Society of the State of New York.

Rocco Joseph Martoccio, MD, Utica. Died July 5, 1986; age 81. He was a 1931 graduate of the University of Rochester School of Medicine and Dentistry. Dr Martoccio was a Fellow of the American College of Allergists and a Diplomate of the American Board of Pediatrics. His memberships

included the American Academy of Pediatrics, the American Academy of Allergy, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

Aaron H. Meister, MD, Hollis. Died July 13, 1986; age 83. He was a 1928 graduate of the University of Maryland School of Medicine, Baltimore. Dr Meister was a Fellow of the American Psychiatric Association and a member of the American Academy of Neurology, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Stanley T. Michael, MD, Ossining. Died July 25, 1986; age 74. Dr Michael was a 1937 graduate of Universita Karlova Fakulta Lékarská, Praha. He was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Psychiatric Association, the Association for Research in Nervous and Mental Disease, the Medical Society of the County of Westchester, and the Medical Society of the State of New York.

Nicholas Neuwirth, MD, Brooklyn. Died July 14, 1986; age 74. Dr Neuwirth was a 1954 graduate of Kossuth Lajos Tudomanyegyetem Orvostudományi Fakultas, Debrecen, Hungary. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Anthony A. Nigro, MD, New York. Died July 22, 1986; age 89. He was a 1923 graduate of New York University College of Medicine, New York. Dr Nigro was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Otolaryngology. His memberships included the Academy of Medicine, the New York Society of Laryngology and Otology, the New York County Medical Society, and the Medical Society of the State of New York.

Samuel Oliver, MD, Lawrence. Died July 24, 1986; age 74. Dr Oliver was a 1938 graduate of Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn, Prussia. He was a member of the American Geriatrics Society, the American Society of Tropical Medicine and Hygiene, the Nassau County Medical Society, and the Medical Society of the State of New York.

John Joseph Pellegrini, MD, Brooklyn. Died July 23, 1986; age 41. Dr Pellegrini was a 1972 graduate of Facoltà di Medicina e Chirurgia Università Degli Studi di Bologna. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

John Anthony Perrone, MD, New York. Died June 3, 1986; age 75. He was a 1944 graduate of Facoltà di Medicina e Chirurgia Università di Torino. Dr Perrone was a member of the American Academy of Family Practice, the New York County Medical Society, and the Medical Society of the State of New York.

Virginia E. H. Pomeranz, MD, New York. Died July 28, 1986; age 61. She was a 1949 graduate of State University of New York Downstate Medical Center. Dr Pomeranz was a Diplomate of the American Board of Pediatrics and a member of the New York County Medical Society and the Medical Society of the State of New York.

Charles R. Pucie, MD, Copiague. Died August 8, 1986; age 75. Dr Pucie was a 1937 graduate of Facoltà di Medicina e Chirurgia Università Degli Studi di Roma. He was a member of the Suffolk County Medical Society and the Medical Society of the State of New York.

Edwin R. Ranzenhofer, MD, New York. Died July 7, 1986; age 57. Dr Ranzenhofer was a 1954 graduate of Yale University School of Medicine, New Haven. He was a member of the American Psychiatric Association, the New York County Medical Society, and the Medical Society of the State of New York.

Samuel Ratowsky, MD, New York. Died April 29, 1986; age 86. He was a 1928 graduate of Boston University School of Medicine. Dr Ratowsky was a Fellow of the American College of Obstetricians and Gynecologists and a member of the New York County Medical Society and the Medical Society of the State of New York.

Werner J. Rose, MD, Kenmore. Died July 15, 1986; age 84. Dr Rose was a 1926 graduate of University of Buffalo School of Medicine. Dr Rose was a member of the Association of Life Insurance Medical Directors of America, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Abraham Marvin Sands, MD, Brooklyn. Died July 28, 1986; age 79. He was a 1932 graduate of New York University College of Medicine, New York. Dr Sands was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Ophthalmology. His memberships included the Academy of Medicine, the New York Society for Clinical Ophthalmology, the American Geriatrics Society, the American Academy of Ophthalmology and Otolaryngology, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Julius Solan, MD, Cliffside Park, New Jersey. Died June 7, 1986; age 83. Dr Solan was a 1927 graduate of Universita Karlova Fakulta Lékarská, Praha. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

Martin Weiss, MD, Binghamton. Died June 28, 1986; age 91. He was a 1919 graduate of State University of New York Downstate Medical Center. Dr Weiss was a member of the Academy of Medicine, the American Academy of Family Practice, the American School Health Association, the Broome County Medical Society, and the Medical Society of the State of New York.

Richard V. Yazmajian, MD, Tenafly, New Jersey. Died August 23, 1986; age 61. Dr Yazmajian was a 1951 graduate of State University of New York Downstate Medical Center. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

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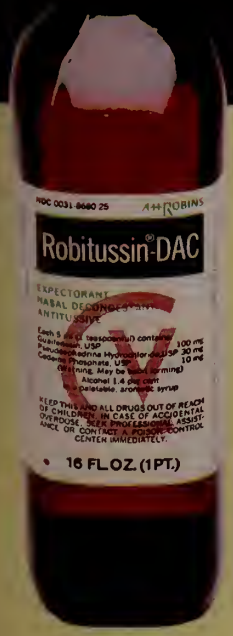

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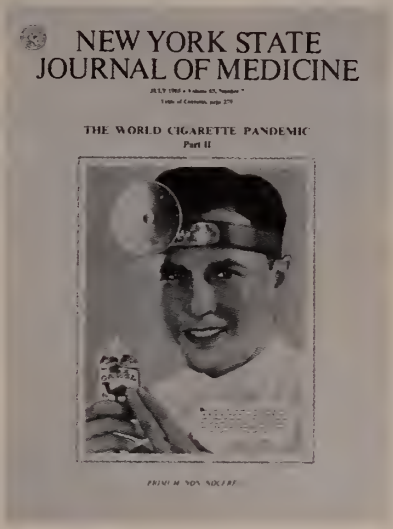

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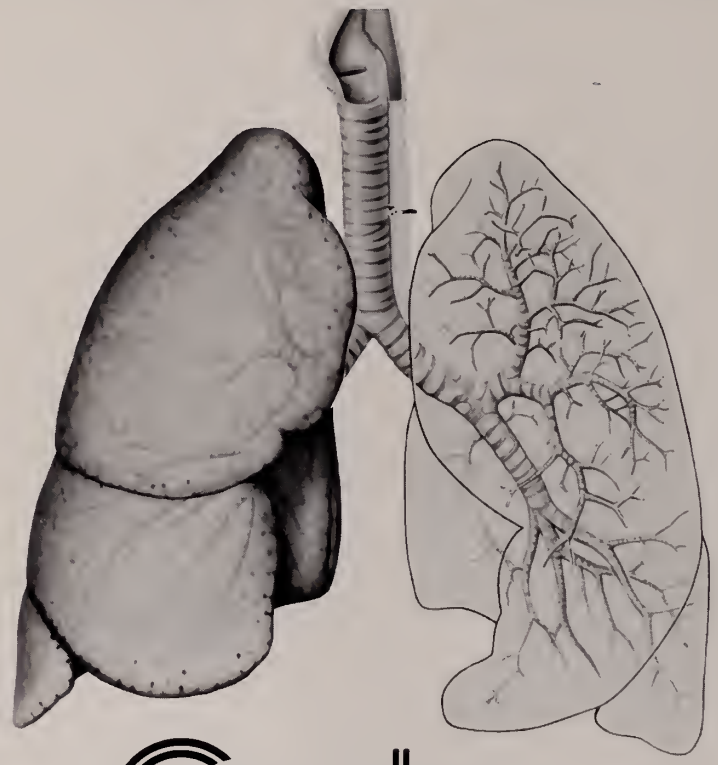

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Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

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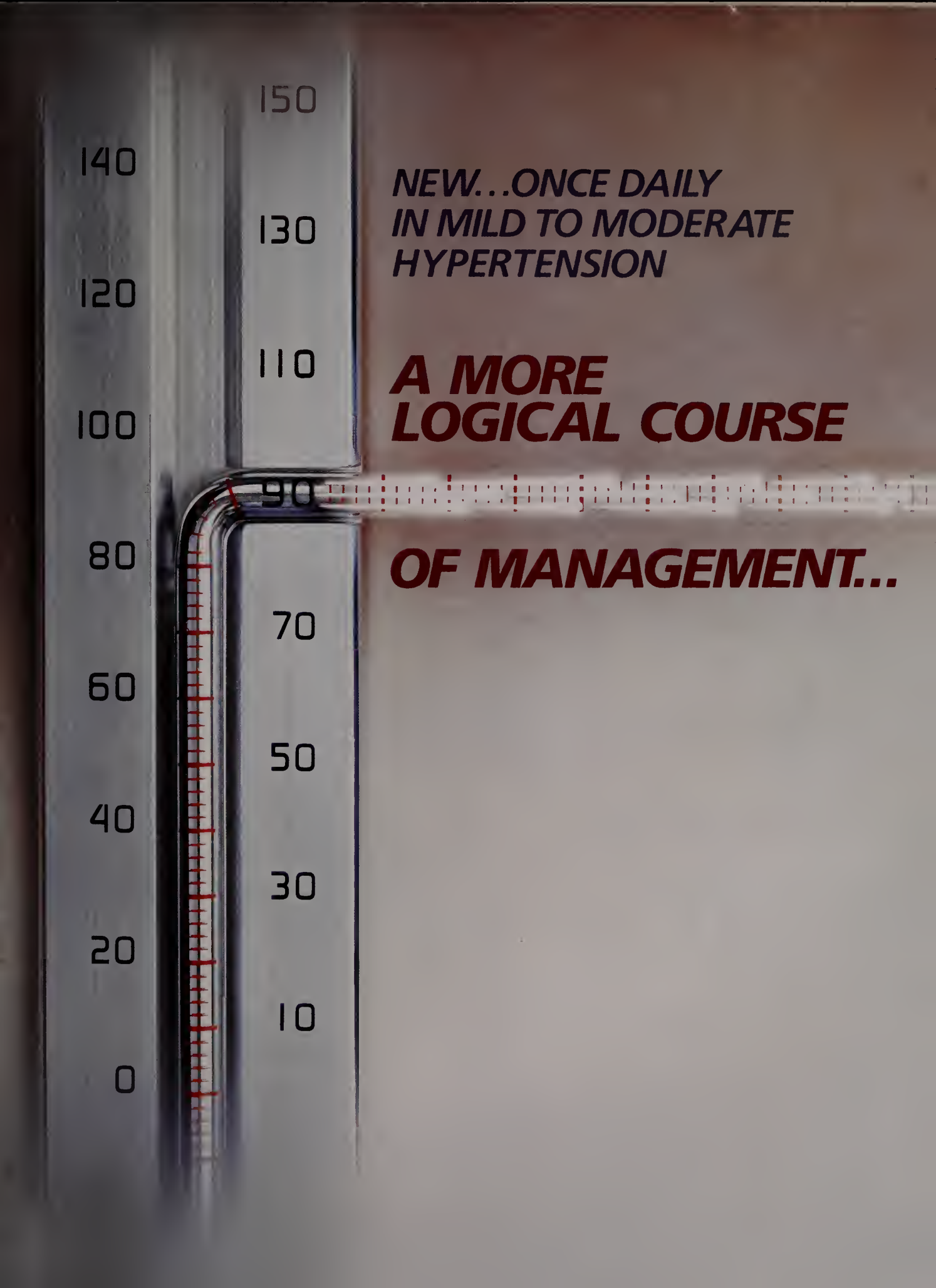
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IN MILD TO MODERATE
HYPERTENSION
A MORE
LOGICAL COURSE
OF MANAGEMENT...

...PROVEN EFFICACY AND A GREATER FREEDOM FROM

***Blanche, R.:** 47, chronic bronchitis, heavy smoker BP 165/105*

***Alice, W.:** 65, overweight diabetic, BP 190/98*

***James, B.:** 38, asthmatic, moderate angina, BP 150/107*

Proven efficacy...

- Reduces diastolic *and* systolic pressure regardless of age or race[1]
- Shown superior to propranolol in several clinical studies[2-4]
- As effective as metoprolol, pindolol, and labetalol[3, 5, 6]

...with established built-in benefits for optimal patient acceptance

- Low incidence of fatigue
- Mental depression, impotence rarely reported
- No adverse effect on potassium, uric acid, lipid, or glucose levels[2, 7-9]
- Safe in COPD and asthmatic patients
- Safe in diabetic patients[10]

ONCE DAILY

SIDE EFFECTS

John, K.: *42, confirmed diastolic BP 102, abnormal lipid profile*

Thomas, G.: *70, asthmatic, drug induced hypokalemia/hyperuricemia, BP 190/98*

Peter, M.: *53, workaholic, chronically fatigued, BP 180/92*

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240 mg scored, sustained-release tablets

Antihypertensive therapy you and your patients can live with

Please see brief summary for contraindications, warnings, precautions, most common side effects, and rates of occurrence.

ISOPTIN...SAFETY BACKED BY OVER 23 YEARS OF WORLDWIDE CLINICAL EXPERIENCE *

Side effects most commonly encountered with ISOPTIN

Constipation	8.4%	CHF or Pulmonary Edema	1.8%
Dizziness	3.5%	Fatigue	1.7%
Nausea	2.7%	Bradycardia	1.4%
Hypotension	2.5%	AV Block (3°)	0.8%
Edema	2.1%		
Headache	1.9%		

Above incidences of adverse reactions derived from clinical trials in 4,954 patients.

Contraindications: Severe left ventricular dysfunction, hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome or second- or third-degree AV block (if no artificial pacemaker is present).

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*Includes eight years of clinical experience in hypertension.

REFERENCES: 1. Cubeddu LX, Aranda J, Singh B, et al: *JAMA* 1986;256:2214-2221. **2.** Leonetti G, Pasotti C, Ferrari GP, et al: *Acta Medica Scand* 1984; suppl 681:137-141. **3.** Data on file, Knoll Pharmaceuticals. **4.** Halperin AK, Kirsten M, Gross PA, et al: *Clin Pharmacol Ther* 1984;36:750-758. **5.** Anavekar SN, Christophidis N, Louis WJ, et al: *J Cardiovasc Pharmacol* 1981;3:287-292. **6.** Anavekar SN, Barter C, Adam WR, et al: *J Cardiovasc Pharmacol* 1982;4:S374-S377. **7.** Lewis GRJ, Steward DJ, Lewis BM, et al: *Int'l Symposium on Calcium Antagonism in Cardiovasc Ther* 1980;270-277. **8.** Leonetti G, Sala C, Bichanini C, et al: *Eur J Clin Pharmacol* 1980;18:375-382. **9.** Midtbo K, Hals O, van der Meer J, et al: *J Cardiovasc Pharmacol* 1982;4:363-368. **10.** Rojdmark S, Andersson DEH: *Am J Cardiol* 1986;57:39D-43D.

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Please see brief summary on following page.

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NEW...ONCE DAILY IN MILD TO MODERATE HYPERTENSION

Brief Summary

ISOPTIN®-SR (verapamil HCl/Knoll) 240 mg scored, sustained-release tablets

CONTRAINDICATIONS 1) Severe left ventricular dysfunction (see WARNINGS) 2) Hypotension (less than 90 mmHg systolic pressure) or cardiogenic shock 3) Sick sinus syndrome or 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker)

WARNINGS **Heart Failure** ISOPTIN should be avoided in patients with severe left ventricular dysfunction (see DRUG INTERACTIONS) Patients with milder ventricular dysfunction should, if possible be controlled before verapamil treatment Hypotension ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension Elevated Liver Enzymes Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported Periodic monitoring of liver function in patients receiving verapamil is therefore prudent Accessory Bypass Tract (Wolff-Parkinson-White) Patients with paroxysmal and or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil While this has not been reported with oral verapamil, it should be considered a potential risk Treatment is usually D C -cardioversion Atrioventricular Block The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia Higher degrees of AV block while infrequent (0 8%) may require a reduction in dosage or, in rare instances discontinuation of verapamil HCl Patients with Hypertrophic Cardiomyopathy (IHSS) Although verapamil has been used in the therapy of patients with IHSS severe cardiovascular decompensation and death have been noted in this patient population

PRECAUTIONS **Impaired Hepatic or Renal Function**: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted in the urine In patients with impaired hepatic or renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSAGE)

Drug Interactions Beta Blockers Concomitant use of ISOPTIN and oral beta-adrenergic blocking agents may be beneficial in certain patients with chronic stable angina or hypertension but available information is not sufficient to predict with confidence the effects of concurrent treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities Digitalis Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted However chronic verapamil treatment increases serum digoxin levels by 50 to 75% during the first week of therapy and this can result in digitalis toxicity Upon discontinuation of ISOPTIN (verapamil HCl) the patient should be reassessed to avoid underdigitalization Antihypertensive Agents Verapamil administered concomitantly with oral antihypertensive agents (e g vasodilators angiotensin-converting enzyme inhibitors diuretics beta blockers prazosin) will usually have an additive effect on lowering blood pressure Patients receiving these combinations should be appropriately monitored Disopyramide Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration Quinidine In patients with hypertrophic cardiomyopathy (IHSS) concomitant use of verapamil and quinidine resulted in significant hypotension There has been a report of increased quinidine levels during verapamil therapy Nitrates The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions Cimetidine Two clinical trials have shown a lack of significant verapamil interaction with cimetidine A third study showed cimetidine reduced verapamil clearance and increased elimination to 1 2 Anesthetic Agents Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics Carbamazepine Verapamil may increase carbamazepine concentrations during combined therapy Rifampin Therapy with rifampin may markedly reduce oral verapamil bioavailability Lithium Verapamil may lower lithium levels in patient on chronic oral lithium therapy Carcinogenesis, Mutagenesis, Impairment of Fertility There was no evidence of a carcinogenic potential of verapamil administered to rats for two years Verapamil was not mutagenic in the Ames test Studies in female rats did not show impaired fertility Effects on male fertility have not been determined Pregnancy (Category C) There are no adequate and well-controlled studies in pregnant women ISOPTIN crosses the placental barrier and can be detected in umbilical vein blood at delivery This drug should be used during pregnancy labor and delivery only if clearly needed Nursing Mothers ISOPTIN is excreted in human milk therefore nursing should be discontinued while verapamil is administered Pediatric Use Safety and efficacy of ISOPTIN in children below the age of 18 years have not been established

ADVERSE REACTIONS Constipation 8 4% dizziness 3 5% nausea 2 7% hypotension 2 5% edema 2 1% headache 1 9% CHF pulmonary edema 1 8% fatigue 1 7% bradycardia 1 4% 3 AV block 0 8% flushing 0 1% elevated liver enzymes (see WARNINGS) The following reactions reported in less than 1 0% of patients occurred under conditions (open trials marketing experience) where a causal relationship is uncertain they are mentioned to alert the physician to a possible relationship angina pectoris, arthralgia and rash, AV block blurred vision cerebrovascular accident chest pain claudication confusion diarrhea dry mouth dyspnea ecchymosis or bruising equilibrium disorders exanthema gastrointestinal distress gingival hyperplasia gynecomastia hair loss hyperkeratosis impotence increased urination insomnia macules muscle cramps myocardial infarction palpitations paresthesia psychotic symptoms purpura (vasculitis) shakiness somnolence spotty menstruation sweating syncope urticaria Treatment of Acute Cardiovascular Adverse Reactions Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately e g intravenously administered isoproterenol HCl levarterenol bitartrate atropine (all in the usual doses), or calcium gluconate (10% solution) If further support is necessary inotropic agents (dopamine or dobutamine) may be administered Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician

OVERDOSAGE Treatment of overdosage should be supportive Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing respectively Asystole should be handled by the usual measures including cardiopulmonary resuscitation

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MEETINGS AND LECTURES

The New York State Journal of Medicine *cannot guarantee publication of meeting and lecture notices unless the information is submitted at least three months prior to the event.*

JANUARY 1987

AROUND THE STATE

MANHATTAN

Jan 8–10. **Retinal Laser Photocoagulation Course.** Manhattan Eye, Ear & Throat Hospital. Contact: Dr Lawrence Yannuzzi, Manhattan Eye, Ear & Throat Hospital, 210 East 64 St, New York, NY 10021. Tel: (212) 838-9200.

NASSAU

Jan 24–25. **Female Urology.** 16 Cat 1 Credits. Long Island Jewish Medical Center. Info: Ann J. Boehme, Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

AROUND THE NATION

ARIZONA

Jan 18–20. **Second International Workshop on Chromosomes in Solid Tumors.** Arizona Health Sciences Center, Tucson. Info: Mary Humphrey, Conference Coordinator, Arizona Cancer Center, University of Arizona College of Medicine, Tucson, AZ 85724. Tel: (602) 626-6044.

Jan 28–31. **Clinical Recognition and Management of Heart Disease—1987.** 17½ Cat 1 Credits. University Medical Center, Tucson. Info: American College of Physicians, PO Box 7777-R-0510, Philadelphia, PA 19175.

CALIFORNIA

Jan 12–16. **The Physician in Management Seminars I & II.** 31 Cat 1 Credits. The Hyatt Islandia, San Diego. Contact: Sherry Mason, American Academy of Medical Directors, 4830 W Kennedy Blvd, Suite 648, Tampa, FL 33609. Tel: (813) 873-2000.

Jan 20–24. **Intensive Course in Geriatric Medicine.** 34 Cat 1 Credits. Miramar-Sheraton Hotel, Santa Monica. Info: American College of Physicians, PO Box 7777-R-0510, Philadelphia, PA 19175.

COLORADO

Jan 24–30. **Update on Pediatric Anesthesia and Intensive Care.** 25 Cat 1 Credits. Beaver Run Resort, Breckenridge. Info: University of Colorado School of Medicine, Office of Continuing Medical Education, 4200 East Ninth Ave, Box C-295, Denver, CO 80262. Tel: (303) 394-5195.

Jan 24–31. **Gastroenterology Update: 1987.** 20 Cat 1 Credits. Lion Square Lodge, Vail. Info: Jean Ryan, Office of Continuing Education, Johns Hopkins Medical Institution, 720 Rutland Ave, Turner 22, Baltimore, MD 21205. Tel: (301) 955-6046.

FLORIDA

Jan 16–18. **Third World Congress of Hysteroscopy.** Fountainebleau Hilton, Miami Beach. Info: Jordan M. Phillips, MD, General Chairman, AAGL, 13021 East Florence Ave, Santa Fe Springs, CA 90670. Tel: (213) 946-8774.

HAWAII

Jan 31–Feb 7. **Infectious Diseases in General Medicine and Pediatric Practice.** 24 Cat 1 Credits. Intercontinental Hotel, Maui. Info: University of Colorado School of Medicine, Office of Continuing Medical Education, 4200 East Ninth Ave, Box C-295, Denver, CO 80262. Tel: (303) 394-5195.

ILLINOIS

Jan 28–31. **The Year in Internal Medicine—1987.** The Drake Hotel, Chicago. Contact: Paula Puntenney, Alumni Center for Continuing Education, Northwestern University Medical School, 301 East Chicago Ave, Chicago, IL 60611. Tel: (312) 908-8533.

(*continued on p 8A*)

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Jan 17–24. **What Is New in Anesthesiology.** 18 Cat 1 Credits. Martinique. Info: George Silvay, MD, PHD, Department of Anesthesiology, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY 10029. Tel: (212) 650-5954.

MEXICO

Jan 19–23. **Diagnostic Radiology Seminars.** 22 Cat 1 Credits. Camino Real, Ixtapa, Mexico. Info: Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Ave, San Francisco, CA 94143. Tel: (415) 476-5731.

VIRGIN ISLANDS

Jan 5–7. **Clinical and Morphologic Aspects of Heart Disease.** 21 Cat 1 Credits. *Jan 8–10.* 19½ Cat 1 Credits. Mahogany Run Golf and Tennis Resort, St Thomas. Info: American College of Physicians, PO Box 7777-R-0510, Philadelphia, PA 19175.

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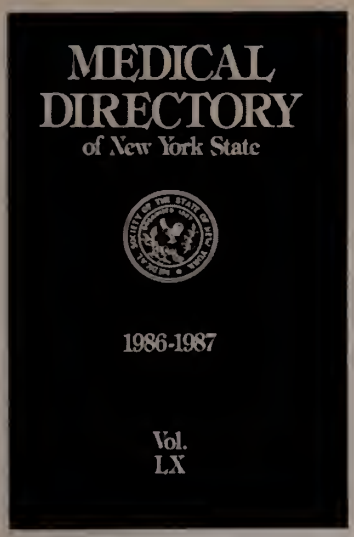

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COMMENTARIES

Aging: A coming of age

Persons aged 65 and older in the United States present a demographic imperative because their numbers are increasing. They now represent close to 12% of the overall population, with persons over 85 constituting the most rapidly growing segment of the population. This latter group is expected to triple in absolute numbers over the next 50 years. Eighty percent of the patients currently living in US nursing homes are over age 80.[1]

Until recently, the elderly with multiple chronic disease states have been largely ignored both in clinical research and consequently in the medical literature. This issue of the *Journal*, however, presents examples of the emerging body of research knowledge pertaining to aging. It addresses the special clinical problems of late life with suggested approaches to their management, and highlights the emerging dilemmas of the application of technology and intensive care when death is imminent.

The body of knowledge of geriatrics is well identified by Charatan[2] in his review of the major psychiatric problems of late life. The special problem of Alzheimer's disease—a silent epidemic—typifies the reasons and need for areas of special study and research among the aged. This as yet incurable and terminal illness places an inordinate burden on families[3] as their beloved relative's personality disintegrates. The subsequent questions of both functional and legal competence further challenge society.[4] The issue of legal competence has particular relevance to the researcher in Alzheimer's disease since the consent for incorporation of the Alzheimer's victim into a research protocol must be obtained from someone other than the patient. Researchers often have difficulty obtaining such consents, particularly for patients in nursing homes,[5] who may not have next of kin who can act on their behalf.

Charatan[2] also highlights the special pharmacological considerations that apply to elderly patients. He points out that multiple alterations in pharmacokinetics and pharmacodynamics accompany aging. These changes are perhaps most readily identified with regard to psychotropic medications such as diazepam. Diazepam, a highly lipid-soluble drug, is metabolized in the liver and excreted by the kidneys. However, by age 75, the proportion of fatty/lipid tissue has doubled at the expense of muscle mass. By age 80, renal function has decreased as much as 50%. Liver metabolism variably diminishes with age and, in addition, hepatic blood flow is significantly reduced. As a result of these changes, there is an increase in the half life of diazepam from 20 hours at age 20 to 90 hours at age 80.[6] Thus, in prescribing for elderly patients, dosages must be reduced and/or the time interval between doses must be increased.

Research methodologies and technological advances as they relate to osteoporosis are well addressed in the article by Firooznia et al.[7] Early diagnosis and a delineation of treatment benefits are critical in regard to this disease. A recent estimate suggests that the health care system incurs an annual cost in excess of $2 billion for the short term management of fractures secondary to osteoporosis.[8] Those elderly persons at risk for both osteoporosis and falling should be identified. This may result in the development of practical preventive strategies, particularly for the group of older women who are at a very high risk of morbidity and mortality from this disease.

The articles in this issue illustrate the rapid development of geriatric medicine. As Charatan[2] notes, the prospect of a specialization in geriatric psychiatry is now receiving support. The American Board of Internal Medicine has formally resolved to offer a certificate of added qualification in geriatrics. These developments validate the unique research base and the special problems and approaches of geriatrics, as well as the necessity for specialized training and education.

Two issues alluded to but not discussed in detail in these articles are the sites at which care for the elderly is provided, and the necessity of an interdisciplinary approach for the management of multiple overlapping chronic diseases and disabilities. Care of the elderly patient in the community setting is generally preferred by both patients and families, but in these instances families may require significant additional supports. The cost of providing such community-based services can rapidly outdistance the

cost of care in a residential health care facility. New options such as day care programs, Medicaid-supported long term home health care, respite programs, and home-based hospice programs are becoming available,[9] and the Medicare home care program has been expanded to facilitate early discharge from hospitals. The elderly, however, tend to suffer under such expedited discharge programs, which result in their being referred in a "quicker and sicker" mode to home care programs or to nursing homes.

The interdisciplinary approach is intended to foster continuity of care, to provide all necessary services efficiently, and to facilitate appropriate placement through gatekeeping programs. Teaching and training in these developing programs is increasingly carried out through a multidisciplinary approach. There is ongoing formal evaluation of the specific roles of allied health professionals and the settings in which they might best care for the elderly. The role of the physician changes to that of medical manager, while the patient's multiple needs are addressed by other team members. The teaching nursing home with community-based geriatric programs is now a recognized site for training and research.

A number of legal, moral and financial issues have assumed importance with regard to the medical care of the elderly. The medicolegal trends in consent to treatment described by Ciccone,[4] and resuscitation policies discussed by Quill et al,[10] demonstrate the range and magnitude of these issues. Morrissey's[11] depiction of financial pauperization consequent to chronic disease in late life is a sobering reminder of the financial implications for the elderly and their loved ones. Health care planners and legislators recognize the costs of aggressive interventions for the elderly.[12] It is perhaps no coincidence that legal methods are being developed and fostered which allow individuals to avoid personal and family financial ruin by opting for death. This is occurring in a society that appears unwilling to either provide or bear the costs of providing medical care for the elderly.

Aging in a sense is coming of age. Future years will witness not only newer technical and therapeutic modalities capable of prolonging life but also the emergence of complex moral, social, legal, and financial issues associated with these efforts.

Medicine and society will have to deal with these matters in an even more intensive manner because they will defy easy resolution. As aging comes of age in a social sense the elderly will have a greater say in these matters and an important place in the conduct of human affairs. This will not be a new development but rather a return to how things once were. Perhaps then we, the young and old alike, will view aging as Robert Browning described it when he wrote in "Rabbi Ben Ezra":

> Grow old along with me!
> The best is yet to be
> The last of life, for which the first was
> made.
> Our times are in his hand.

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Where are we going with "do not resuscitate" policies?

Whenever there are technologic advances in medicine, there are necessarily questions concerning their appropriate use. Cardiopulmonary resuscitation (CPR) is a noteworthy exception to this statement. Questions about CPR concern the appropriateness of *not* using it. Developed as a means to respond to sudden, unexpected cardiac or respiratory arrest, CPR has given rise to a technologic imperative that mandates its use and which has spawned a sizable body of medical, legal, and bioethical literature, as well as institutional policies and procedures pertaining to decisions not to use it. In New York State, the Governor's Task Force on Life and the Law has even issued a proposal for legislation governing such decisions.[1]

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The article in this issue of the *Journal* by Quill et al[2] describes one institution's experience with its policy regarding decisions about CPR and other resuscitation methods. It provides a timely opportunity for a retrospective and prospective view of the development of "do not resuscitate" (DNR) policies.

This editorial commentary asserts that there are no new or special legal principles regarding resuscitation decisions, nor is there any need for any. It maintains that development, clarification, and refinement of medical standards regarding resuscitation decisions are properly the responsibility of the medical profession and are not appropriate matters for legislation. It examines the utility of institutional policies and procedures regarding resuscitation decisions, and points to some indications of future developments regarding resuscitation decisions.

The law has long recognized the important distinction between medical decision making by physicians and personal decision making by patients. In modern-day law, the informed consent doctrine embodies this distinction by delineating the physician's responsibility to disclose information and the patient's responsibility to consent to or refuse treatment.[3] Through the exercise of medical judgment, the physician forms a diagnosis or differential diagnosis and determines the medically appropriate course of action. After this medical decision making has taken place, the physician informs the patient about diagnosis, prognosis, the recommended course of action and its risks and expected benefits, and treatment alternatives. Thus informed, the patient must either accept or reject the proposed course of action.

Under the law, resuscitation decisions are not different from other medical decisions. It is incumbent upon the physician to decide, in accordance with accepted medical standards, which resuscitation methods, if any, should be offered for each patient. Then it is incumbent upon the patient to consider the array of medically appropriate alternatives and to either accept or reject them. There is no valid legal reason to presume that resuscitation is required for every patient, with the narrow exception of a bona fide medical emergency.

In its lengthy report proposing DNR legislation, the New York State Task Force on Life and the Law begins by stating that "medical choices are moral choices."[1] This erroneous statement may reflect the thinking at the root of the confusion regarding the legality of DNR orders. Medical choices are medical choices, and existing law recognizes them as such. It may be stimulating or interesting to discuss moral questions that technology presents, but it is not useful to confuse them with established legal or medical principles. Resuscitation legislation is inappropriate because it necessarily narrows existing provider and patient rights, because it confuses physicians and the public by making some think that those rights do not exist without a statute, and because it usurps the medical profession's responsibility to establish standards for medical decision making.

Establishing accepted medical standards is and always has been the responsibility of the medical profession, whether it is the accepted standard for prescribing antibiotic therapy or for instituting resuscitation efforts. The mechanisms for this process are in place: scientific and medical research, evaluation, reporting in the medical and scientific literature, and developing consensus. The process is not served by enactment of a DNR statute.

An obvious next question is whether the development of medical consensus is aided by institutional policies regarding resuscitation decisions. It is beyond the space and conceptual limitations of this commentary to speculate at length on the genesis of such policies. A variety of factors culminated in the pervasive but inaccurate belief that resuscitation was legally required for every patient whose cardiac or respiratory function ceased, regardless of its clinical indication. Nonetheless, many physicians recognized this as illogical and verbally instructed staff not to initiate resuscitation for certain patients. Discomfort with this practice inevitably led to the development of institutional guidelines for determining the resuscitation status of each patient.

The first generation of these policies was based on the presumption that every patient should be resuscitated unless a written order specified otherwise. Some of these policies contained consent provisions. The major focus of these early policies was to provide for documentation and communication of each patient's resuscitation status.

A second generation of DNR policies evolved, reflecting a recognition that mere designation of "DNR" was too broad and did not allow for consistency in utilizing differing levels of resuscitation methods for different patients. The policy described by Quill et al[2] is of this type. Policies such as this evidence a clearer understanding that resuscitation is not appropriate for every patient, and that for those patients for whom intervention is appropriate, there is a need to determine what level of intervention is indicated. Nonetheless, these policies paradoxically still require that the patient consent to *not* having an intervention which is not medically appropriate, rather than recognizing the patient's right to consent to or refuse an intervention which is medically appropriate.

The potential utility of carefully written institutional policies regarding resuscitation decisions is multifold. First, such policies encourage uniformity in terminology and consistency in response by minimizing confusion about the specific interventions to be implemented. The old "Code Blue" type of designation provided no guidance as to which measures should be applied or how far resuscitation efforts should go, and left much to individual interpretation of the designation. Second, such policies can provide a clear mechanism for communication of a patient's resuscitation status. Third, these policies can enhance accountability for medical decision making by providing requirements for documentation, including both a written order and an explanatory progress note. Finally, the policies can provide an opportunity for review and evaluation as a means of contributing to the ongoing process of clarifying and refining medical standards.

Indications of future directions can be seen. Two official statements were recently issued, more clearly acknowledging the distinction between medical and personal decision making. The first is the American Hospital Association's Policy and Statement, "The Patient's Choice of Treatment Options,"[4] calling for institutional methods to assure the patient's right and responsibility to select among treatment options. The second is the 1986 State-

ment of the American Medical Association Council on Ethical and Judicial Affairs, "Withholding or Withdrawing Life-Prolonging Medical Treatment,"[5] emphasizing the patient's choice as controlling, even when this conflicts with what the physician deems medically appropriate. Both of these statements point out the need for carefully drawn guidelines regarding patients lacking decisional capacity.

These indicators will be reflected in future policies. Indeed, a third generation of institutional policies is already emerging in the long term care setting. These are "patient treatment preference" policies, which focus on the patient's right to refuse treatment. Typically, they provide for a determination upon admission of the patient's express preferences regarding medical treatment, including resuscitation, and also provide guidelines for decisions about patients lacking decisional capacity.

Further refinement of existing institutional policies will likely lead to a broader emphasis on the patient's right to choose among medically appropriate alternatives, and away from the view that special rules apply to resuscitation decisions.

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Health care for the elderly: The road to poverty

The scenario is becoming a typical one: An elderly couple have been married for decades. The husband becomes chronically ill and the wife can no longer care for him. Thus the husband must be placed in a skilled nursing facility. The couple own their own home on which there is still a mortgage, and they have managed to save a total of $10,000 during the course of their marriage. Together, they have income of $1,950 a month. The husband receives $500 a month from Social Security and $1,200 a month from a pension. The wife receives $250 a month from Social Security. Because the couple cannot afford the costs of the nursing home, they turn to the Department of Social Services (DSS) for assistance.

DSS informs them that in order to qualify for Medicaid, most of the husband's income will have to be used to defray the costs of the assistance provided to him. The wife (the "community spouse") will have to live on the amount allowed to welfare recipients. When she tells DSS that she simply cannot live on that amount, she is told that the law specifies that this is the maximum to which she and her husband are entitled. However, the wife may also qualify for various welfare programs if she becomes sufficiently destitute.

Under this scenario, the elderly wife will lose her home because she will not be able to make the mortgage payments, and will be forced to find a new home where she can live on the amount permitted to a public assistance recipient.

In many cases this unfortunate result may be avoided by informed advocacy on behalf of the elderly. Physicians and other health care providers who work with the elderly must become more knowledgeable in regard to the entitlements of their patients (or know where to refer their patients for help) in order to assure that this highly vulnerable population is not wrongly deprived of the opportunity to live out their lives in dignity.

Under New York State law, there are steps that the wife can take to protect herself. The legal obligation of a spouse to pay for the medical debts of the other is specifically limited by his or her financial ability to do so. Thus, the wife may simply refuse to pay over any of her income for the health care costs of her husband, and Medicaid may not refuse to accept the husband for Medicaid as a result. Medicaid may, however, proceed against the community spouse for some contribution to the costs of caring for the husband. This is done by filing a support proceeding in the family court. However, it is unlikely that a family court judge would require the community spouse to pay over an amount that would result in her becoming destitute or in needing public assistance.

A court may require that a community spouse make some financial contribution to the extent that her income and resources exceed her needs. For example, in *Department of Social Services v Barbara M.*,[1] DSS sought to force a community spouse to apply her entire life savings of approximately $70,000 toward the support of her husband, who was in a nursing home and receiving Medicaid. Her income, including interest earned on her bank accounts, totaled $9,000 per year; her expenses totaled $8,040 per year.

The court stated that it must be "mindful of guarding the public purse. . .A proper balance must be struck between the ever present need to reduce the public burden and the equally important need to be humane, and allow [a community spouse] to maintain a reasonable degree of dignity and self-reliance in her own remaining years. To

strip her of everything she and her husband have accumulated during their years of marriage would be an affront to the conscience of the Court, and would very soon require that [the community spouse] herself become a public charge." Thus, the court ordered that she did not have to exhaust her bank accounts, but rather would be required to pay $440 a month towards the medical costs of her husband.[1]

Of course, the refusal to make contributions to a spouse's health care costs does not help the community spouse who does not herself have the necessary resources to survive, but there is another step the community spouse can take to prevent her destitution. She can bring a support action in family court in order to obtain some of the institutionalized spouse's income for her own support. Such support actions are not classical adversary proceedings between estranged spouses. Indeed, the institutionalized spouse will rarely contest the action, and usually will be supportive of it. Rather, the battle will be between DSS and the community spouse.

For example, in *Septuagenarian v Septuagenarian*,[2] the community spouse sought support of $1,125 a month from her husband of 50 years, who was in a nursing home. The community spouse was "devoted to her husband and his care and visit[ed] him several times a week at the nursing home." The court ordered that the support be paid and noted that without the help, "[elderly] women will be forced from their homes, deprived of even their modest life styles and relegated to a life of grinding poverty."

But the most important step that the elderly can take is to plan in advance for the need for chronic health care, and then to take appropriate estate planning steps in order to prevent destitution should a spouse require nursing home care. There are a number of measures people can take to assure that their homes, life savings, or other resources will not be lost to catastrophic health care costs. When a person is about to enter a nursing home, it may be too late to take action.

On numerous occasions elderly people have been required to totally deplete their income and resources in order to pay for the health care costs of a spouse in a nursing home. Oftentimes such demands are illegal or inappropriate. Elderly people, faced with the fact that they are about to institutionalize their spouse, often are so emotionally distraught that they are unable to adequately represent their own interests, and passively comply with such demands even if it means their own destitution.

Indeed, even the informed elderly spouse may need support in order to take the steps necessary to prevent impoverishment. It is tragic that, in order to prevent destitution, a community spouse should have to refuse to contribute to the costs of a spouse's health care, or even sue in family court for support. Many of the elderly see this as the antithesis of their lifetime of devotion and commitment to their marriage. They must know how to protect themselves and their spouses from poverty, and have the support needed to enable them to follow through with those protective steps.

Increasingly, support and legal organizations are being formed to protect the rights of the elderly. The legal services program and several law schools in New York City have established legal clinics devoted exclusively to the protection of the legal rights of the elderly. Where neither of these is available, the elderly can often be well served by seeking out knowledgeable private attorneys. Also, many community groups have been formed to assist the elderly. These groups may provide direct services or may serve as an invaluable referral resource. Finally, many local governments have also established offices for the elderly which may be of assistance. While it may be unrealistic to expect physicians to be well versed in the fine details of Medicaid law, they can nevertheless serve as a valuable resource for their patients by providing them with basic information and referrals to advocates. The physician who works with the elderly must take an affirmative role in helping to assure that health care for the elderly is not the road to poverty.

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1. *Department of Social Services v Barbara M.*, 474 NYS 2d 193 (Fam Ct Dutchess Cty, 1984).
2. *Septuagenarian v Septuagenarian*, 483 NYS 2d 932 (Fam Ct Queens Cty, 1984).

The effect of a community hospital resuscitation policy on elderly patients

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ABSTRACT. A resuscitation policy was instituted at a 384-bed community teaching hospital in Rochester, NY. The policy gave patients the option of four levels of care in the event of a life threatening emergency: critical care; limited critical care; conservative care, and comfort oriented care. A retrospective chart review was used to compare six-month periods before and after implementation of the policy. For patients over 80 years of age who died while in the hospital, the findings were as follows: a significant increase in the use of explicit orders by attending physicians to limit resuscitation ($p < 0.001$); a possible increase in the use of the intensive care unit for those patients classified in the critical care category ($p < 0.1$); and a nonsignificant decline in the use of cardiopulmonary resuscitation overall. For those patients over 80 years of age who left the hospital alive and had discharge diagnoses of cerebrovascular accidents, metastatic cancer, or organic brain syndrome, the policy resulted in a significant increase in explicit orders to limit resuscitation efforts only among the patients who had suffered cerebrovascular accidents ($p < 0.025$). Hospital resuscitation policies can help physicians share with their patients the burden of limiting resuscitation and offer patients increased self-determination and more appropriate utilization of medical technology during this period in their lives.

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Policies that allow patients the option of not being subjected to cardiopulmonary resuscitation (CPR) attempts in the event of a life threatening emergency have been the subject of considerable debate[1-6] and the focus of a presidential commission.[7] There is general agreement that such decisions are within the province of the physician-patient relationship, with the guiding force always being the patient's expressed wishes.[1-8] Hospitals have been directed to develop formal policies to guide the physician in limiting resuscitation efforts. The attending physician must write explicit orders to limit resuscitation attempts and must document in the medical record the reasoning used to arrive at such a directive.[9-12]

A multidisciplinary team at The Genesee Hospital, a 384-bed community-based teaching hospital in Rochester, NY, developed the following protocol allowing patients the option of differing levels of care for use in a life threatening medical emergency:

- Critical care—maximal therapeutic effort without technologic restraint
- Limited critical care—maximal ordinary and temporary extraordinary therapeutic measures short of sustained cardiopulmonary resuscitation. The attending physician must specify which extraordinary measures to include and which to exclude in such an emergency
- Conservative care—all ordinary therapeutic measures, but no cardiopulmonary resuscitation or extraordinary measures should be initiated
- Comfort oriented care—therapeutic efforts are guided by maximizing the patient's comfort regardless of their effect on the disease process.[13]

The protocol required that, to be implemented, any order limiting resuscitation had to be written in the order section of the patient's medical record by the attending physician. If nothing were written, the patient would automatically be treated according to the criteria of critical care. It was recommended that the attending physician document the manner in which the patient's wishes for limited resuscitative efforts were determined.

The purpose of this research was to explore the impact of such a protocol on the explicit ordering of resuscitative limits by physicians, the actual performance of CPR, and the utilization of the intensive care unit. The first group of patients studied included all patients over 80 years of age who had discharge diagnoses of cerebrovascular accident, organic brain syndrome, or metastatic cancer. This group was selected based on the belief that many of these elderly patients with chronic diseases would choose resuscitative limits if they were offered. The second group of patients studied were those more than 80 years of age who had died in the hospital. This group was selected to determine whether CPR had actually been performed at the time of death, and to compare these findings with physicians' orders about resuscitation.

We wish to emphasize that, in our opinion, not all elderly patients should have limitations placed on their care,

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but rather that many of these patients might choose less than what critical care entails if they were offered alternatives. There is also good documentation in the medical literature demonstrating the futility of cardiopulmonary resuscitation and other extraordinary measures in elderly patients with chronic debilitating diseases.[14-17]

A review of patients' charts was undertaken for all patients in these study populations that had been admitted to The Genesee Hospital during comparable six-month periods before and after implementation of the resuscitation policy. The study sought to test the following hypotheses:

- The policy will result in the increased use of explicit written orders to limit resuscitation in all four study groups.
- The overall use of cardiopulmonary resuscitation will decline slightly among patients over 80 years who subsequently died, but its use for those patients in the critical care category will increase.
- The overall use of the intensive care unit will decline slightly among patients over 80 who subsequently died, but its use for those in the critical care category will increase.

Patients and Methods

The resuscitation protocol was instituted at The Genesee Hospital on January 1, 1983. Prior to that time there was no formal policy to guide attending physicians in the appropriate limitations of therapeutic efforts, even if a patient had requested such limitations. The Genesee Hospital is a 384-bed community based teaching hospital affiliated with the University of Rochester School of Medicine and Dentistry. The six-month comparison periods were from July 1, 1982 to December 31, 1982 and from July 1, 1983 to December 31, 1983. During the last three months of 1982, the policy was under active discussion by the medical attending staff but had not yet been implemented.

The study populations were identified from the hospital computer records. They included all patients during these time intervals who were more than 80 years of age and who died while in the hospital, and all patients more than 80 years of age who were discharged with a diagnosis of cerebrovascular disease, organic brain syndrome, or metastatic cancer. These patients' charts were identified and reviewed retrospectively. The patient's sex and insurance status were recorded from the front data sheet of the medical record. Since most patients in these groups were retired, it would have been difficult to ascertain their socioeconomic status from the medical record other than by evaluating their insurance coverage. All order sheets were then reviewed for the presence of any orders to limit resuscitation. Designations of the three categories within the protocol that limited resuscitation in any way (limited critical care, conservative care, and comfort oriented care) were recorded, as were other notations such as "do not resuscitate" (DNR) or "no heroics." All progress notes were then reviewed for any indication that resuscitation was to be limited, and to identify the individual who wrote the note or order. The charts were also reviewed to see if the patient had been sent to the intensive care unit and, if the patient died, to see if CPR had been attempted.

Chi-squared analysis was used to compare the sex and insurance status of the patients who had limits placed on resuscitative measures with those who did not, as well as those patients who went to the intensive care unit and/or received cardiopulmonary resuscitation. The same type of analysis was used to compare the ordering of resuscitative limits, the use of the intensive care units, and the use of cardiopulmonary resuscitation for the two six-month time intervals.

TABLE I. Chart Documentation of Orders to Limit Resuscitation for Patients Over 80 Who Died in the Hospital

Time Interval	Physician Orders on Order Sheets	Progress Notes Only	Total of Orders and Progress Notes Only	Critical Care—No Orders for Limitation
July 1, 1982–December 31, 1982	23/107 (21%)	38/107 (36%)	61/107 (57%)	46/107 (43%)
July 1, 1983–December 31, 1983	59/83 (71%)	6/83 (7%)	65/83 (78%)	18/83 (22%)
χ^2 value of differences*	46.8	21.0	9.5	9.5

* Critical chi-square with one degree of freedom = 3.84.

Results

Between 1982 and 1983, there was a significant ($p < 0.001$) increase in the use of explicit orders to designate limitations for resuscitation among patients over 80 years of age who subsequently died in the hospital (Table I). The largest differences were found in the third-quarter comparisons (1982 = 1/46 (2%) versus 1983 = 20/35 (57%); $\chi^2 = 31.1$), and in the fourth-quarter comparisons (1982 = 22/61 (36%) versus 1983 = 39/48 (81%); $\chi^2 = 22.3$). Surprisingly, there was a significant increase in the frequency of orders to limit resuscitation between the third and fourth quarters of 1982, before the policy was formally implemented (third quarter = 1/46 (2%) and fourth quarter = 22/61 (36%); $\chi^2 = 18.3$). There was a statistically significant ($p < 0.001$) decrease in the number of charts in which notations to limit resuscitation were found only in the attending physician's progress notes during the two time periods. The overall recording in the chart (order sheets and/or attending progress notes) of plans to limit resuscitation also increased significantly ($p < 0.005$). The remaining patients for whom resuscitation limitations were not noted in the orders or progress notes were assumed to be in the critical care category.

Table II shows comparisons—by resuscitation status as defined in the hospital chart—of the actual performance of CPR on patients over 80 years of age who died while in the hospital. This comparison demonstrated a significant decrease ($p < 0.005$) in the number of orders for full cardiopulmonary resuscitation (critical care by the above criteria) between the two time intervals (1982 = 46/107 (43%) versus 1983 = 18/83 (22%); $\chi^2 = 9.5$). The decrease in the actual number of cardiopulmonary resuscitations performed was not statistically significant ($\chi^2 = 1.55$). There was no significant change between 1982 and 1983 in the probability that cardiopulmonary resuscitation would be performed when critical care was ordered or when limitations were ordered. Of the patients who were given CPR when limitations had been ordered, half in 1982 and three quarters in 1984 were in the limited critical care category. As can be seen in Table III, there was no significant change between 1982 and 1983 in the utilization of the intensive care unit for patients over 80 years of age who died in the hospital. There was also no change between 1982 and 1983 in the probability of the patient's going to the intensive care unit when there were written orders to limit resuscitation. There

TABLE II. Cardiopulmonary Resuscitation (CPR) Performance According to Level of Care for Patients Who Died in the Hospital

Level of Care Orders	CPR Performed	No CPR Performed	CPR %
Critical care			
July 1, 1982–December 31, 1982	24	22	52
July 1, 1983–December 31, 1983	10	8	55
Limitation to resuscitation			
July 1, 1982–December 31, 1982	2	59	4
July 1, 1983–December 31, 1983	4	61	6

TABLE III. Intensive Care Unit (ICU) Visits According to Level of Care Orders for Inpatients Over 80 Who Died

Level of Care Orders	Went to ICU	No ICU	ICU %
Full critical care			
July 1, 1982–December 31, 1982	7	39	15
July 1, 1983–December 31, 1983	5	13	28
Limitation to resuscitation			
July 1, 1982–December 31, 1982	13	48	21
July 1, 1983–December 31, 1983	14	51	22

was, however, a trend suggesting a statistically significant ($p < 0.1$) increase in the likelihood of going to the intensive care unit with full resuscitation orders (critical care) ($\chi^2 = 2.99$).

Table IV summarizes the review of the order sheets and progress notes for notations of any limitation of resuscitation efforts for patients over 80 years of age who left the hospital with the discharge diagnosis of either cerebrovascular accident, organic brain syndrome, or metastatic cancer. None of these patients underwent CPR while in the hospital. No statistically significant differences were found between 1982 and 1983 in the writing of orders or progress notes indicating plans to limit resuscitation for patients with organic brain syndrome or metastatic cancer. However, there was a statistically significant ($p < 0.005$) increase between 1982 and 1983 in the use of orders to limit resuscitation among patients who had suffered cerebrovascular accidents. The decline in the use of progress notes only among this group of patients was also statistically significant ($\chi^2 = 4.8$; $p < 0.05$). With the combination of orders and progress notes, there remained a significantly ($p < 0.025$) increased use of resuscitative limits among these patients between 1982 and 1983 ($\chi^2 = 5.2$).

There were no significant differences in the orders to limit resuscitation or in the actual use of CPR or the intensive care unit when the patients' sex or insurance status was compared.

Discussion

Implementation of an explicit resuscitation policy by The Genesee Hospital in January 1983 resulted in a significant change in the ordering behavior of the attending staff. The policy was associated with a statistically significant increase in the use of explicit written orders by attending physicians to designate limitation of resuscitation attempts in patients over 80 years of age who subsequently died in the hospital. There were also fewer charts in which the plans to limit resuscitation efforts were documented only in the progress notes and not in the order sheets. This decline did not offset the overall increase in explicit orders to limit resuscitation. When these two factors were combined, there was an overall increase in the percentage of patients whose charts had some designation to limit resuscitation efforts. There was also a significant increase in explicit orders to limit resuscitation between the third and fourth quarters of 1982, prior to implementation of the new policy. Coincidentally, the new terminology (limited critical care, conservative care, and comfort oriented care) began to appear in the charts during the fourth quarter of 1982, when the policy was simply being discussed but before it was officially implemented. This suggests some contamination of the 1982 data that may have led to an underestimation of the actual change in physicians' ordering behavior stimulated by the policy.

As is shown in Table II, the actual number of cardiopulmonary resuscitation procedures performed decreased between 1982 and 1983. Since there was no change between 1982 and 1983 in the probabilities that CPR would be performed when critical care was ordered (0.52 versus 0.55) or when limitations were ordered (0.04 versus 0.06), this decline reflects a change in ordering practice. The fact that CPR was performed only 50–55% of the time when critical care was ordered in this study group suggests that unwritten forms of communication must still be used by some attending physicians in spite of the hospital policy requiring explicit documentation in the chart for any limitation on resuscitation. Also disturbing is the fact that six patients (two in 1982 and four in 1983) were resuscitated in spite of their documented desire not to be resuscitated. An investigation of why this occurred revealed that four of the six patients were classified as limited critical care, and the physician's orders were either unclear or misunderstood. As a result, an order form has been developed so that critical care can be ordered explicitly rather than inferred by the absence of other orders, and so that the attending physician can address whether or not CPR should be performed for patients in the limited critical care category.

There was no change in the overall use of the intensive care unit for patients over 80 years of age who died in the hospital during the study periods in 1982 and 1983. However, there was a trend suggesting that the probability that patients with orders for full resuscitation (critical care) would go to the intensive care unit increased between 1982 and 1983. This is consistent with more appropriate use of the intensive care unit for patients who wish full critical care, though usage remained low.

For patients over 80 years of age who did not die in the hospital and who had either organic brain syndrome or metastatic cancer, the policy had no statistically significant impact. However, resuscitation limitations were ordered more frequently in 1983 than in 1982 for patients over 80 years of age who left the hospital after suffering a cerebrovascular accident. There was also a significant decrease in the use of progress notes only to document resuscitation plans, but this did not offset the overall increase in orders (order sheets plus progress notes only) to limit resuscitation, which remained statistically significant. Since the odds that CPR will actually be performed in an emergency situation differ according to these orders, this

TABLE IV. Chart Documentation of Orders to Limit Resuscitation for Patients Over 80 Who Left the Hospital Alive with Diagnoses of Organic Brain Syndrome, Cerebrovascular Accident, or Metastatic Cancer

	Organic Brain Syndrome		Cerebrovascular Accident		Metastatic Cancer	
Chart Documentation	1982	1983	1982	1983	1982	1983
Orders	7/29 (24%)	8/26 (31%)	2/32 (6%)	14/28 (50%)	5/27 (19%)	9/28 (32%)
Progress notes only	4/29 (14%)	0/26 (0%)	5/32 (16%)	0/28 (0%)	2/27 (7%)	0/28 (0%)
Total	11/29 (38%)	8/26 (31%)	7/32 (22%)	14/28 (50%)	7/27 (26%)	9/28 (32%)

* The remaining patients in each group who had no orders for resuscitative limits were assumed to receive critical care.

change in ordering behavior may have a profound effect on what actually happens to these patients in a life threatening emergency.

Developing, implementing, and studying resuscitation policies such as this one developed by The Genesee Hospital Resuscitation Committee should be a requirement for all hospitals. Not only are physicians legally required to document a resuscitation plan in the order section of the chart,[18,19] but for moral and ethical reasons they must provide patients with the option of not being resuscitated.[1-8] This policy is still in use by the staff of The Genesee Hospital, who have found that it offers them and their patients more and better options, depending on the patient's disease state and wishes. When the patient's wishes cannot be ascertained,[20] the course is less clear. If the patient's wishes are clear, however, then it is imperative for the physician to carry them out. Physicians should help patients face these difficult issues, so that the patient's wishes become the guiding force. Many physicians have done this for years, communicating the plan in whispers to the nursing staff and avoiding putting anything in writing in order to protect themselves legally. Now, however, the law states that physicians can (and must) provide explicit documentation in the medical record.

It is legal to limit resuscitative efforts if that is what the patient, with knowledge of his or her condition, desires. Philosophers and ethicists have also been supportive of efforts to give patients the option of setting limits on their treatment. The policy presented here provides options for both the physician and the patient that reflect differing approaches to therapy, depending on the patient's age, the state of the disease, and the patient's belief system. By increasing the patient's options, and by being as explicit as possible about the course of treatment, physicians can increase a patient's sense of control over his or her destiny.

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See also pp 618–620.

Clinical utility of bone mineral content measurements in the diagnosis and treatment of osteoporosis

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Osteoporosis is the most common metabolic disease of bone. In the United States, it affects as many as 20–30%, or more, of white postmenopausal women older than 65 years. As the relative number of elderly persons in the population steadily increases, osteoporosis is also expected to increase in frequency. At the present time, osteoporosis is a major cause of morbidity and disability in the elderly, often resulting in fractures of the spine, hip, or other bones, consequent to a minor trauma.[1-7] Recently, there has been renewed interest in the prevention and treatment of osteoporosis because of encouraging results reported with estrogen treatment, exercise, and dietary calcium supplementation, and, in our opinion, the successful treatment regimen for patients with osteoporosis based on Frost's concepts of bone physiology and pathology.[2,8-12]

To obtain the most satisfactory results from these measurements, the diagnosis of osteoporosis must be made before spontaneous fractures occur. In normal bone, there is a continuous process of new bone formation and bone resorption. In most instances, osteoporosis results when there is a disturbance in the optimal coupling of these processes, resulting in a predominance of bone resorption.[2,13,14] Clinically, osteoporosis may be defined as the diminution of bone mass per unit volume of bone to a level below that required for adequate mechanical support, resulting in structural bone failure (ie, fracture). Thus, the clinical diagnosis of osteoporosis is usually not made until late in the course of the disease—often after a fracture has developed.[15,16] Measurement of the quantity of trabecular and cortical bone in critical anatomic sites, such as the spine and hip, is helpful in the assessment of baseline bone mass. Serial measurements can determine the rate of bone loss, enabling identification of subjects at risk for early osteoporosis due to low bone mass and/or rapid bone loss.

MEASUREMENT OF BONE MINERAL CONTENT

A number of techniques are available for measuring bone mineral content (BMC), including radiography, single and dual photon absorptiometry, and quantitative computed tomography.[17-23]

Radiography. Assessment of the status of the skeleton using roentgenograms is the oldest technique available. It is most useful in the diagnosis of conditions that lead to subperiosteal and intracortical bone resorption, such as hyperparathyroidism. In subjects with spinal osteoporosis, generalized loss of density, paucity of trabeculae, and, in more advanced stages of the disease, deformities and compression fractures of the vertebrae may be noted. Measurement of the cortical thickness of peripheral tubular bones is also a simple and reproducible procedure and is useful as a gross indicator of the general status of the cortical bone in the body. However, in general, cortical bone is not a sensitive indicator of bone loss, at least in the earlier stages of osteoporosis. Furthermore, osteoporosis cannot be detected on conventional roentgenograms until at least 20%[15] to 30%[16] of bone mass is lost.

Single Photon Absorptiometry (SPA). This technique[17] is widely available and is simple to perform. The radioactive component is usually ^{125}I (27.5 KeV). The photon beam is passed through the bone and the surrounding tissues. A detector is positioned on the opposite side of the part being examined (Fig 1). SPA systems are usually calibrated to provide measurements in g/cm (grams of bone per length). SPA may be used for measurement of diaphysis (essentially an integral of cortical bone) or metaphysis (an integral of cortical and trabecular bone) of the tubular bones of the extremities.

The procedure has an accuracy rate of approximately 6% and a precision level of 2–3%.[18] The precision in the metaphysis may be significantly less because of difficulty in precise repositioning. SPA is useful in clinical research, but is probably of limited value for individual patients because of an overlap in measurements between the subjects with and without osteoporosis. This overlap occurs even if the extreme distal radius, which contains significant amounts of trabecular bone, is utilized. Recent evidence indicates that trabecular bone mineral content of the distal radius correlates poorly with iliac crest trabecular bone volume (TBV) (measured by histomorphometry) and with spinal trabecular BMC.[19]

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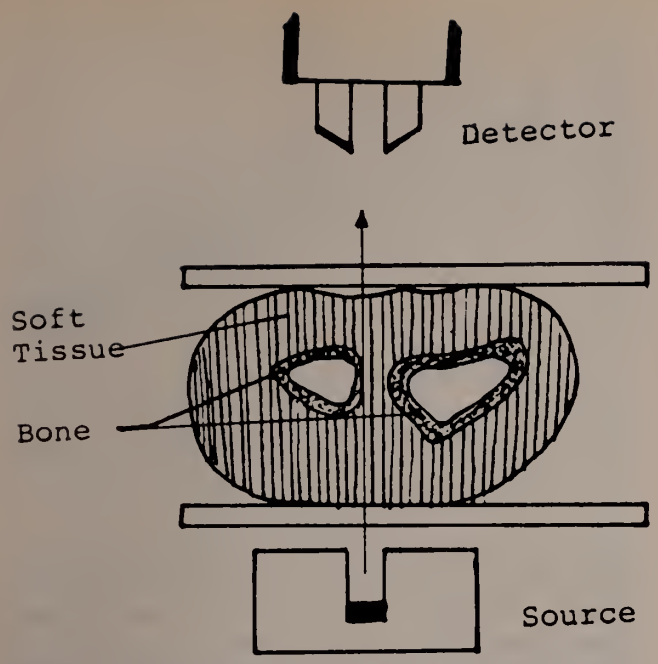

FIGURE 1. Schematic diagram showing the set-up for photon absorptiometry.

Dual Photon Absorptiometry (DPA). This technique[18,20] is becoming more readily available because of commercial introduction of dedicated DPA units. The radiation source used is ^{153}Gd (44 KeV and 100 KeV). As in SPA, a projectional scan is obtained with the photon beam passing through the body and hitting the detector assembly mounted on the opposite side. DPA systems are usually calibrated to provide measurements in g/cm^2—grams of bone per unit area scanned. DPA may be used for measurement of cortical bone of the extremities or integral bone of the spine, extremities, and other bones.

The most significant advantage of this technique is its superior accuracy in measuring integral bone density. This advantage exists because, unlike computed tomography (CT), DPA is only minimally affected by the presence of fat in the measured volume. The accuracy in phantoms is about 1–2% and in vertebral specimens about 6–15%.[18] To date, DPA has been more successful than CT in measuring integral bone density in the hip region. This is important because hip fracture is the most clinically significant complication of osteoporosis. Although the risk of hip fracture may not depend significantly on the quantity of bone present in the neck of the femur, nevertheless this is an important factor. Thus, measurement of integral bone density and the rate of bone loss in the femoral neck may be helpful in predicting the risk of hip fracture. If this hypothesis is proven, then these assessments may prove to be the most important contribution of DPA.

Unlike CT, DPA cannot spatially separate cortical from trabecular bone. Thus, it may not be useful for evaluating the early stages of trabecular bone loss in the spine. The earliest manifestation of spinal osteoporosis is seen as loss of trabecular bone that leads to vertebral fractures. CT is the best method to measure purely trabecular bone of the vertebrae. The values provided by DPA represent quantities per surface area scanned. Thus, all the calcified tissues in the path of the beam, including the dense cortical bone of the laminae, facets, pedicles, vertebral endplates, and cortex, as well as osteophytes and calcifications of the aorta, are included in the measured volume, in addition to the trabecular bone of the vertebral body. Although DPA provides accurate measurements, what it measures, with respect to the spine, is not a representative indicator of spinal trabecular bone. Therefore, DPA is of doubtful value for detection or prediction of the risk of spinal trabecular bone loss.

Quantitative CT for Measuring Trabecular Bone of the Spine

Bone loss in most forms of osteoporosis probably occurs simultaneously in trabecular and cortical bone. However, the rate of trabecular bone loss is several times that of cortical bone, probably because trabecular bone has a faster turnover rate. Consequently, trabecular bone is a more suitable measurement site and a more sensitive indicator of bone loss, particularly in the initial phases of osteoporosis. Clinically, the earliest osteoporotic fractures occur in regions composed predominantly of trabecular bone: the body of the vertebrae and distal radius. Trabecular bone loss is the predominant early manifestation of postmenopausal osteoporosis, estrogen-deficiency states such as oophorectomy and premature ovarian failure, long term corticosteroid excess—both endogenous and exogenous—and immobilization.[1,2,7–13]

By providing an axial cross-sectional map of x-ray absorption coefficient values through the vertebral body, CT has enabled the spatial separation of trabecular bone from cortical bone; each can now be measured independently.[8,21–23] Computed tomographic measurement of BMC requires reliable calibration of the scanner and meticulous attention to technique. It should only be performed with CT scanners that have provisions for correction of geometric distortion and beam hardening and that can provide reliable measurements in the range of values of trabecular bone. CT measurements are made with the help of a bone mineral calibrating device that contains reference densities with densitometry characteristics similar to those of bone and soft tissues (Fig 2). We measure 3–4 cm^3 of purely trabecular bone at the midportion of four vertebrae, usually T12-L3.

Further details of this technique and the values for subjects with and without osteoporosis have been reported.[22,23] The accuracy rate of the technique in measuring the mineral content of fresh cadaver vertebrae utilizing a specially constructed anthropomorphic torso phantom is 4–6%.[22] The precision level for serial in vitro and in vivo measurements, with a GE9800 CT/T, is 1.4% and 1.8%, respectively.[24]

The most important advantage of CT is the three-dimensional localization of cortical and trabecular bone, yielding a density measurement of a predetermined volume of trabecular or cortical bone. This is essential when testing the spine, where inclusion of the dense cortical bone of the vertebral elements in the measured volume, as occurs with DPA, may interfere with the measurement of purely trabecular bone. Another advantage of CT is its ability for precise repositioning. In the spine, for example, exactly the same area must be measured on serial measurements. Precise repositioning is assured with CT via a

FIGURE 2. **Top,** a lateral localizer view of the spine showing positioning for CT measurement of BMC. **Bottom,** an axial slice through the body of L2.

lateral localizer view and computerized measurements along the axis of the spine.

The accuracy of measurements obtained with CT decreases when there is an unusually large amount of fat present in the vertebrae. Dual energy CT is helpful in alleviating this problem;[25,26] however, it yields less precise measurements. The accuracy of CT measurements can be improved by using a correction factor to compensate for the effect of vertebral fat content.

Normal Bone Mass and Age-Related Physiologic Bone Loss

Many factors, including race, heredity, sex, diet, and exercise affect bone mass.[1,7] The total body bone mass increases steadily from birth to about age 30, when skeletal maturity and peak bone mass are reached. Bone mass may stay fairly constant to age 40 or so, or it may slowly decrease. After age 40, men lose bone (spinal trabecular) at the rate of 0.4–0.6% per year, while women, in general, lose bone at the rate of 1–2% per year (Figs 3,4).[18,22,27]

Pathologic Bone Loss

Several conditions, including long term corticosteroid administration, Cushing's disease, oophorectomy, hyperparathyroidism, immobilization, nutritional deficiencies, and early menopause are associated with various degrees of bone loss.[1,2,7,8,16,28] An important, but often unrecognized, factor is restriction of dietary calcium. A recent

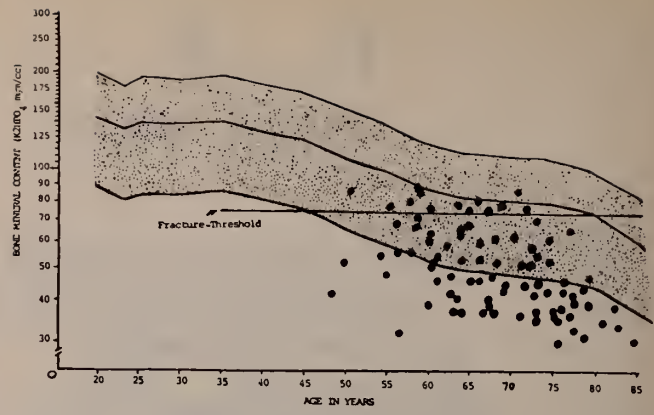

FIGURE 3. Individual measurements of spinal BMC in 89 women with osteoporotic vertebral fractures. The center line depicts mean spinal trabecular BMC in 419 women, with 90% confidence limits shown.

study[29] found an association between deficiencies in oral calcium intake and higher fracture ratios at all ages. Apparently, when there is long term dietary calcium deficiency, this deficiency is compensated for by removal of calcium from the person's own skeleton. We have noted a fairly high rate of osteoporosis in lactase-deficient subjects[30] who habitually avoid milk—one of the most significant sources of calcium in the diet. When a low-calcium, high-protein, high-phosphate diet is maintained for many years, as is currently the fad with some young Americans, it may lead to low total body bone mass. Women at increased risk for osteoporosis commonly have blue eyes, blond hair, and a petite frame. Acquired risk factors include being underweight and smoking cigarettes.

Clinical Utility of Measurement of BMC

Measurement of trabecular spinal BMC has several uses. It can identify subjects with low spinal trabecular bone mass, who may be in danger of developing early spinal osteoporosis.[2] It can be used to establish a diagnosis of osteoporosis (prior to occurrence of fracture). In addition, it can help to quantify the extent of osteoporosis.

Serial (yearly) measurements are helpful in identifying apparently healthy subjects with rapid bone loss.[2,20] Quantitative evaluation of the response to preventive or therapeutic measures is also possible. Serial measurements also aid in predicting the risk of bone loss associated with corticosteriod therapy or other therapeutic regimens.

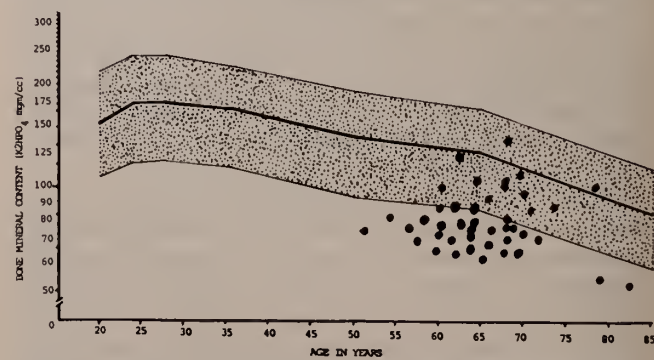

FIGURE 4. Individual measurements of spinal BMC in 43 men with osteoporotic vertebral fractures. The center line depicts mean spinal trabecular BMC in 339 men, with 90% confidence limits shown.

In our studies, in approximately 5–7% of apparently healthy, white perimenopausal women (47–53 years old), vertebral trabecular BMC values were only slightly above the fracture threshold. Assuming continuation of bone loss, these subjects may soon cross the fracture threshold, even if they lose bone at a normal rate; they are, therefore, at probable risk for early spinal osteoporosis. Clinical diagnosis of osteoporosis has been an all-or-none phenomenon; the diagnosis is made only when a fracture develops consequent to a minor trauma. But osteoporosis does not develop overnight, and a diagnosis of asymptomatic osteoporosis—characterized by an altered physical state of bone—should be made, whether a spontaneous fracture is present or not. The existence of osteoporosis as a continuum should be acknowledged.

Fracture Threshold

Although bone strength is not entirely dependent on the mineral content of bone, it is an important factor. Thus, it has been assumed that beyond a certain level, defined as the fracture threshold, bone is prone to spontaneous fracture.

The overall strength of vertebrae is dependent on both cortical and trabecular bone. There is a strong correlation between spinal trabecular BMC and the fracture threshold.[18,23,31] One can determine the vertebral fracture threshold by CT measurement of spinal trabecular BMC with a high degree of confidence. Some investigators have reported a good correlation between DPA measurement of integral spinal density and fracture threshold, while others have reported a poor correlation. Further comparative studies of DPA and quantitative CT are needed.

The vertebral fracture threshold can be correlated with the likelihood of fracture occurrence. Alternatively, a specific level of spinal BMC or integral spinal mineral can be selected, and the percentage of subjects with spontaneous fractures falling below this level can be determined. Some investigators have chosen the fifth[20] or the tenth[32] percentile of integral spinal mineral as the cutoff point for normal subjects, or a specific quantity of spinal BMC[18,27] as the fracture threshold. In our clinical practice, we use the fifth percentile of spinal BMC for normal premenopausal women (45 years old) as the vertebral fracture threshold.[23] We have found 84% of female patients with spontaneous vertebral fractures to have spinal BMC values below this level. When this criterion is used to evaluate the BMC of the spine, a significant number of healthy older women would be classified as having osteoporosis.

Assessment of the Rate of Bone Loss

Measurement of the rate of spinal trabecular bone loss by CT is important in subjects who may be losing bone due to specific forms of treatment. In these patients, when serial measurements reveal spinal BMC values approaching the fracture threshold, it may be prudent to consider other therapeutic measures, if available. Another potential application of serial measurement of spinal trabecular BMC by CT is identification of perimenopausal women who are rapidly losing bone. In our studies, approximately 38% of healthy perimenopausal women (47–53 years old) lose bone at a rate of about 5.5% per year. The rate of bone loss in the remaining 62% of women is slightly less than 2% per year. It is assumed that this accelerated rate of bone loss reverts to the normal 1–2% rate in a few years. Nevertheless, during this interval, a significant amount of bone may be lost. Thus, the risk of spinal osteoporosis may be predicted by CT measurement of the baseline quantity and the rate of loss of spinal trabecular bone in perimenopausal women. If this hypothesis can be proven, then identification of perimenopausal women at risk of spinal osteoporosis has important clinical implications, including selection of women who are candidates for preventive measures and those who are in need of early postmenopausal estrogen replacement.

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An overview of geriatric psychiatry

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Aging seems to have acquired a new respectability, helped no doubt by President Reagan's having reached the age of 75 recently. Ronald Reagan is the oldest person ever elected President. His vitality may be contrasted with that of William Henry Harrison, the oldest-ever President at that time, who died in office from pneumonia in 1841 at the age of 68. That occurred one month after his inauguration, when he had rejected the advice of his aides to wear an overcoat. President Reagan has survived a bullet in his lung and resection of skin and colon cancers; he wears a hearing aid. His great personal popularity helps send us the message that aging is alive and well in America today.

That message is good news for geriatric psychiatry, the growth and importance of which can be measured in several ways. In May 1978, 15 psychiatrists established the American Association for Geriatric Psychiatry. Today, the association numbers 650 members and represents the fastest growing subspecialty in psychiatry. Already, there is support for certification in geriatric psychiatry—analogous to the existing certification in child psychiatry—by the American Board of Neurology and Psychiatry. The increasing interest in geriatric psychiatry is underscored by the large number of meetings, symposia, and courses devoted to the subject both in the United States and abroad. Books and articles on the three major psychiatric illnesses in old age—delirium, dementia, and depression—appear so often that it is hard to keep track of the expanding data base in this field. Although federal funding for training and research has been cut back under the Deficit Reduction Act, private foundations are becoming more interested in geriatric psychiatry. The political impact of senior citizens themselves cannot be ignored. Spokesmen for this minority—to which we shall all one day belong—are raising their voices throughout the land, demanding that the elderly receive their fair share of mental health services.

ISSUES IN GERIATRIC PSYCHIATRY

Of primary importance to geriatric psychiatrists is the recognition of the relationship of somatic disease to mental disorder in old age. Delirium, for example, is a common complication of somatic disease in the elderly. The British geriatrician John Agate stated, "As a sign of acute physical illness in old age, mental change is more significant than a rise of temperature or pulse rate, and often, it gives useful warning of a more insidious disease."[1]

The reasons for the frequency of delirium in old age are complex. They include reduced cerebral reserve; the British use the term acute brain failure as an alternative to the historic term delirium. Bodily homeostasis is more easily upset in later life, so that dehydration, electrolyte imbalance, incipient diabetic coma, renal failure, and altered hemodynamic status during surgical intervention may all contribute to delirium. Sensory impairments—deafness, and reduced vision from cataracts, glaucoma, and macular degeneration—interfere with incoming stimuli and isolate the deaf or poorly sighted elder from his peers. Sensory deprivation can contribute to delirium when the aged mind produces its own fantasies, delusions, and hallucinations to compensate for the reduction of sensory input from the outside world. This phenomenon is sometimes called the sundowner syndrome.

A second issue in geriatric psychiatry is the increasing prevalence of organic disease of the brain, with or without obvious clinical manifestations. Sir Martin Roth put it well: "In earlier life, organic psychoses are comparatively rare; in old age they are commonplace and their manifestations so protean that they can never be omitted from consideration when arriving at a diagnosis."[2] DSM III* provides a comprehensive classification and description of organic mental disorders, including ten specific organic brain syndromes. Geriatric psychiatry is faced with the serious public health problems of senile dementia of the late Alzheimer type and multi-infarct dementia, which together account for 87% of all cases of dementia in old age. Geriatric psychiatrists must also seek out the elusive one patient in eight who suffers from dementia with a potentially reversible or treatable cause.

A third factor of concern to geriatric psychiatry is the importance of the social network, especially the informal network, in supporting the mentally impaired old person in the community. We all carry in our mind's eye the image of the boy scout helping the old lady across the road. This image reflects an age-old truth: A civilization is measured by how it cares for its aged members. Studies have shown the greater value and effectiveness of the informal caring network in this regard. This is not meant to minimize the importance of the geriatric evaluation team or of the devoted professionals who serve old persons in their homes. But the professional who must use time efficiently operates in a different framework than the neighbor who brings a covered dish dinner to a frail, confused old wom-

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* *Diagnostic and Statistical Manual of Mental Disorders*, ed 3. Washington, DC, American Psychiatric Association, 1980.

an who lives alone, or the daughter who comes in to help her partially paralyzed father. Making diagnoses, preparing reports, and prescribing psychotropic medications are indispensable factors in treating the elderly. But the home health aide, the caring grandchild who visits regularly, and the church volunteer who is willing to spend time conversing or playing gin rummy all contribute to the support and well-being of the socially isolated, mentally impaired elderly person.

A fourth issue in geriatric psychiatry is that the psychopharmacologic treatment of the geriatric patient is quite different from that of the younger patient.[3] Pharmacodynamics and pharmacokinetics alter with age. In geriatric patients, there is altered absorption of psychotropic drugs, and excretion is prolonged due to reduced renal blood flow, irregular filtration rate, and tubular secretion. Cardiac output falls with a consequent increase in drug circulation time. In addition, the elderly exhibit a loss of muscle in relation to fatty tissue, and since most psychotropic drugs are lipid-soluble, the drugs tend to accumulate to a greater extent. Plasma protein levels also decline with age, so the total binding of drug to plasma protein also decreases, resulting in more unbound drug to affect the target organ, the brain. Liver metabolism too may be altered, resulting in a longer half-life of the drug. Finally, the brain of an older person has undergone changes; neurons may have dropped out in a variable pattern, altering the effects of a drug and crucial feedback systems. Thus, patients in their 70s and 80s may experience side effects from many drugs up to seven times as often as do patients in their 20s.

The geriatric psychiatrist knows that doses of psychotropic agents must be one third to half those used in younger patients, and that the dose must be gradually increased, while the patient is kept under close observation. The motto of the geriatric psychiatrist must always be "start low, go slow." Salzman[4] has pointed out the value of antidepressant blood levels and of the electrocardiogram in monitoring the treatment of geriatric patients suffering from depression.

Fifth and finally, geriatric psychiatry is well served by the return of psychiatry to the mainstream of medicine. Without underestimating the importance of psychodynamic and social factors in the mental disorders of old age, geriatric psychiatrists are daily reminded that the brain is the organ of the mind. Thus, advances in the understanding of the biochemistry and neurophysiology of behavior, and in techniques such as medical imaging of the brain as well as new techniques like positron emission tomography (PET), offer exciting prospects for the understanding of changes in mood and memory with age. Internists and family physicians are the psychiatrist's allies in treating hypertension and atherosclerosis—the primary causes of stroke, which results in so much mental disability. Further, the dramatic success achieved in the treatment of patients with Parkinson's disease with levodopa gives hope that replacement therapy in certain forms of depression associated with old age—specifically, those involving neurotransmitter deficiencies—might offer more lasting relief than is achieved using antidepressants.

The joke that the American psychiatrist no longer sits behind his couch taking notes, but wears a white coat and even a stethoscope to convince his patients that he is a real medical doctor, applies even more forcibly to geriatric psychiatry. While geriatric psychiatrists accept the theoretical basis of psychodynamic and psychosocial models, in practice they rely more on psychotropic medications and somatic approaches to treatment of elderly patients.

Senile Dementia of the Alzheimer Type

The frontier of knowledge about senile dementia of the late Alzheimer type is advancing rapidly. It is estimated that about 2.5 million people suffer from this disease. The disease is the fourth most common cause of death in the US today. Dr Daniel Cowell of the National Institute of Aging wrote, "Of the total population of 23.5 million persons 65 years of age or older in the US in 1977, 4.8% resided in nursing homes. Of these, a minimum figure of 32% represents those patients who were considered to have some type of senile dementia (360,000 patients)."[5]

Little is known about risk factors for senile dementia; however, it is known that the prevalence rises to more than 20% in persons over the age of 80. This suggests that age per se may be the primary risk factor. Does this mean that senile dementia might be a hereditary disease controlled by genes expressed late in life? If this were true, it could mean that everyone would develop Alzheimer's disease provided they lived long enough. Larsson and his coworkers[6] in Sweden in 1963 showed that the siblings of index cases of senile dementia had a 4.3 times greater chance of developing the disease than a nonrelated population of the same age. Some family studies in the US have reported possible increased risk for the development of senile dementia among first degree relatives of patients, especially parents and siblings. In a review of 13 studies on familial risk, Matsuyama and colleagues[7] at UCLA found that in 22% of families there was at least one additional affected member. Only 11.4% of the families exhibited transmission through two or more generations.[7]

Individuals with Down's syndrome, if they survive beyond age 40, almost all develop senile plaques and neurofibrillary tangles. The excess chromosome 21 carries a predictive value for the later development of Alzheimer's disease.[8] So far, chromosomal studies in Alzheimer's disease have not yielded consistent results.[9]

PET scans of patients with senile dementia, using 18-fluoro deoxyglucose, have demonstrated cortical hypometabolism, especially in the parietal and temporal lobes.[10] This temporo-parietal hypometabolism may be specific enough to be an important diagnostic aid in senile dementia of the Alzheimer type; diagnosis is currently made by a process of exclusion. The amount of metabolic decline is correlated with the degree of dementia.[11]

Biochemical studies of neurotransmitter systems have shown that in senile dementia, the cholinergic as well as the noradrenergic, serotoninergic, and somatostatin systems are involved. A recent review article discusses in more detail the search for biologic markers in Alzheimer's disease.[9] Aluminum has been suggested as a factor in neurofibrillary degeneration in senile dementia, in Down's syndrome, and in dialysis dementia. The theory suggesting a slow virus as the cause of senile dementia is still viable, although it has not been possible to transmit Alzheimer's disease to animals, including primates. Research

into the cause of senile dementia is advancing on many fronts, and a breakthrough cannot be far off.

Depression in Old Age

Depression is the most common mental disorder after the age of 65. It used to be thought that individuals inevitably became more depressed as they aged; that old age was a sad and despondent time, full of wintry longings for a vanished youth. However, recent surveys by the National Institute of Mental Health demonstrated that the prevalence of major depressive episodes among the community-based elderly population was significantly less than that found at earlier stages of the life cycle. DSM III criteria for major depression apply to the elderly as well as to other age groups. There are some significant differences in geriatric depression: apathy is more common than agitation; the prevalence of paranoid symptoms is higher; and these symptoms disappear with alleviation of the depression. Depression is often masked in the elderly, with hypochondriasis an important symptom complex. In the elderly depressed hypochondriac who goes from doctor to doctor, a differential diagnosis may be difficult, because the geriatric patient may be suffering from chronic somatic disease as well as depression.

Depression in the elderly is a serious public health problem, illustrated by the fact that the suicide rate among aged white males is three to four times that of the population as a whole. As far as causation of depression in old age is concerned, this period of life has been aptly termed "the season of loss"; losses, moreover, which are rarely compensated by gains, as they are during earlier life. Therefore, a major problem for older people is coming to terms with loss. The two losses that most often result in depression are loss of a love object, usually a spouse, and loss of health. The alarming frequency with which the death of one spouse follows that of the other after a few weeks or months has been called the broken heart syndrome, and is evidence of the lethal effect of severe grief in the survivor. The mechanism is thought to be coronary thrombosis triggered by stress. Loss of health, including disabling somatic disease such as arthritis, chronic cardiac failure, stroke, and peripheral vascular disease with amputation, often leads to depression. Loss of mobility is particularly devastating to the geriatric patient, possibly because it is perceived symbolically as the forerunner of that final immobility which is death. Similarly, a fall in a geriatric patient is much more serious than when it occurs in a younger patient. Even when it does not result in a fracture or serious injury, a fall often has an effect out of all proportion to the physical consequences. It seems to undermine the old person's security, leading to anxiety and depression, which may continue long after the event.

Other losses, whether real, fantasized, or merely threatened, contribute to depression in the elderly. Among these are retirement, sensory losses like deafness and failing vision, and loss of income resulting in fear that the aged person will outlive his or her financial resources. And the aged person whose beauty, physical accomplishments, and prestige are eroded by time is more vulnerable to depression.

Lasch[12] has been critical of what he calls the culture of narcissism which adversely affects the aged:

> This irrational terror of old age and death is closely associated with the emergence of the narcissistic personality as the dominant type of personality structure in contemporary society. Because the narcissist has so few inner resources he looks to others to validate his sense of self. He needs to be admired for his beauty, charm, celebrity or power—attributes that usually fade with time. Unable to achieve satisfying sublimations in the form of love and work, he finds that he has little to sustain him when youth passes him by. He takes no interest in the future and does nothing to provide himself with the traditional consolations of old age, the most important of which is the belief that future generations will in some sense carry on his life's work. Love and work unite in a concern for posterity, and specifically in an attempt to equip the younger generation to carry on the tasks of the older. The thought that we live on vicariously in our children (more broadly, in future generations) reconciles us to our own supersession—the central sorrow of old age, more harrowing even than frailty and loneliness. When the generational link begins to fray, such consolations no longer obtain.

Thus Lasch confirms clinical experience: Those persons whose self-concept depends on qualities that are diminished by age are more likely to become depressed. For them, old age is a threat to their integrity.

In the elderly, depression must be differentiated from dementia. It was hoped that the dexamethasone suppression test (DST) would help distinguish between depression and dementia. Unfortunately, in the dementias of old age, the rate of nonsuppression rises to about 50%.[13] Thus, the DST is not specific enough to be of value in differentiating between depression and dementia.

A similar difficulty exists with the computed axial tomographic (CAT) scan. The CAT scan is useful in demonstrating cerebral atrophy, whether cortical or ventricular. But in healthy, aged volunteers given CAT scans, about 16%, or one in six, showed enlargement of the cerebral ventricles beyond age expectations. Thus, in a depressed elderly subject, cognitive impairment may be apparent and may be reversible with proper treatment. If this so-called "pseudodementia" happens to be accompanied by radiologic atrophy, diagnostic errors may result. In such cases, it is prudent to determine whether there is a history of one or more depressive episodes, and to take into account the presence of marked affective symptoms in reaching a diagnosis. In doubtful cases, a therapeutic trial of an antidepressant is always worthwhile; in true cases of depression, improvement in mood and disappearance of symptoms will occur beginning in 10–14 days, while in dementia, the patient will likely become more confused.

Psychotherapy

Is psychotherapy possible with the elderly? Age should not by itself stand in the way of psychotherapy, if one believes that change is possible right up to the end of life. However, certain barriers need to be overcome. First, the psychiatrist should have come to terms with his own aging, and should have freed himself from agism, the concept first developed by Robert Butler.[14] Working with the aged stimulates fears about one's own aging, recalls old conflicts with one's patients, frustrates the psychiatrist seeking dramatic therapeutic successes, and may cause anxiety in the doctor whose basic philosophy is that the aged will die soon anyway, and, worst of all, may die during his treatment.

Second, deafness may be a big barrier in working with

the elderly. In the interest of avoiding wasted time, the psychiatrist's opening statement should always be, "Can you hear me?" Poor vision is also a common problem. When a younger, fully sighted patient mentions a significant dream or begins to describe some episode of dynamic importance, the therapist's attentiveness increases, which the patient immediately perceives. This does not occur with the poorly sighted elderly; rather, easily seen and unequivocal cues must be sent out by the therapist.

Third, amnesia can contribute to the elderly patient's tendency to become repetitive. It is a common experience with the elderly to find that they bring up material over and over again. This is partly due to their forgetting that they had shared the same material with the therapist on an earlier occasion.

Fourth, garrulousness has often been observed among the elderly. Is this an unconscious attempt by the old person to hold on to human relationships, or does it represent an effort at mastery? Another possible interpretation is that garrulousness reflects the anxiety of the aged, who feel that time is running out for them. The therapist must recognize that time is not on his side; one cannot afford the luxury of unlimited time as with younger patients, for intercurrent disease or even death may put an abrupt end to one's therapeutic efforts.

Fifth, it is necessary to limit the duration of psychotherapy sessions. One reason is that older patients need to visit the bathroom more frequently. In addition, older patients are often not able to sit attentively for 50 minutes, hence sessions should be made shorter.

Finally, there is the issue of transference. Usually, the psychiatrist is the same age as or older than the patient. With geriatric patients, the psychiatrist is often younger, and may unconsciously take on aspects of the patient's child or grandchild. When the psychiatrist gratifies the patient's unconscious needs, he will be regarded as the good child. When he frustrates the patient, he will be equated with the bad child who will not comply with parental wishes. Transference can lead to real struggles between the older patient and the younger psychiatrist, and these problems may play a part in noncompliance when psychotropic medications are prescribed. It is recommended, therefore, never to challenge the geriatric patient who finds it necessary to belittle the psychotherapist. The experienced psychiatrist will permit the patient to take up a position of superiority or dominance when necessary. The patient will derive some benefit from the fantasized superiority and will return for the next session, his self-esteem reinforced. It is also important never to dissolve the transference.

Preventing Mental Disorder in Old Age

Recommendations about the prevention of mental disorder at any age are often met with skepticism, yet the national policy on aging has a very simple main goal: "to provide the elderly with the maximum opportunity to live an independent and healthy life and to encourage them to remain in the economic and social mainstream." To address this goal, the White House Conference on Aging is held every ten years—the last one was held in 1981. A report of its conclusions, with 668 recommendations, was sent to the president and the congress. A few of these recommendations, if followed, would have a major impact on some mental disorders of the elderly. For example, stopping smoking, proper exercise and nutrition, weight control, proper rest, and reduction of salt in the diet could all help reduce the incidence of hypertension and, consequently, stroke. The 26% reduction between 1964 and 1975 in the number of men who smoke and the reduced per capita consumption of milk, butter, cream, ice cream, and eggs, coupled with the more aggressive diagnosis and treatment of hypertension, have resulted in a 22% decline in deaths from heart disease between 1968 and 1977. This lowered incidence of heart disease suggests a favorable effect on cerebrovascular disease as well.

An increasing volume of literature from both health and social studies suggests the need to prevent social isolation and loneliness among the elderly. In communities across the US, senior centers, operating under private or public auspices, offer a range of programs for the elderly. A well-run senior center can protect many of its members from depression brought on by social isolation, lack of stimulus, and inferred rejection. The senior center offers elders the opportunity to serve their peers, with the gratification and increase of self-worth that follows. A few years ago, studies at the National Institutes of Health[15] with elderly male volunteers showed that longevity correlated positively with the complexity and degree of organization of the day's activities.

Much has been written about retirement and its impact on the final years. Researchers have stressed the importance of remaining involved and in training during the later years to preserve mental health. It is unrealistic for anyone to live on for 15–25 years of retirement with nothing to do, with no purpose in getting up each day, and with no future goals. That was stated forcefully by the 18th century poet William Cowper: "Absence of occupation is not rest; A mind quite vacant is a mind distress'd."

In conclusion, the prevention of depression in old age requires a real change of attitude in society towards the elderly—a change which will guarantee every older person the right to work and to love. That was Sigmund Freud's formula for mental health, elegant in its simplicity. Erik Erikson taught that the theme of old age was the maintenance of integrity. Nowhere was this better expressed than in Ernest Hemingway's masterpiece *The Old Man and the Sea*. This epic tale, set in the Caribbean, described how Santiago, an old fisherman, was defeated but not destroyed. Hemingway, who had a great fear of old age, once said, "As you get older, it is harder to have heroes, but it is sort of necessary." That insight should inspire a note of optimism for the final years.

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FROM THE LIBRARY

THE NEUROPSYCHIATRIC DISORDERS OF THE AGED

Life is a continuous process, and despite the classification of people into groups according to their chronologic ages, there is no clear-cut boundary line between any two groups. However, age distinctions are made for practical purposes, and those who have reached the age of sixty-five are placed in the aged group. Since the span of life has been increased by approximately twenty years during the first half of this century, the aged have become more and more numerous. . . .

Aging is a biologic process, and it is characterized by anatomic, physicochemical, physiologic, and psychologic changes. Physically it is characterized by a steady and progressive decline in all functions. The central nervous system shows a tendency towards increase in glial elements, and the nerve cells undergo considerable sclerosis. Senile plagues and Alzheimer fibrillary changes in nerve cells are present even in the brains of many normal old people. The autonomic nervous system likewise shows changes in the neural elements, and this results in inadequate functional activities of the various organs of the body. Cerebral vascular changes result in diminished efficiency of that system, causing some anoxia and interference with the adequate supply of nourishment to the nerve cells and with the lymphatic drainage of the brain. Muscle power is diminished, and motor disabilities are not uncommon. The equilibrium is generally impaired. There is definite dulling in sensory perception. Deafness is not uncommon in old people, and this produces an additional handicap by making them somewhat suspicious and even paranoid. The cardiovascular system does not function as efficiently as in the young. The glands of internal secretion likewise undergo changes. Sex glands decrease their hormonal output. The pituitary shows an increase in the chromophobe cells and a decrease in the acidophils. Myxedema is not infrequent. The entire gastrointestinal tract shows degenerative changes; the teeth fall out, the mucous membranes atrophy, secretions of the stomach, pancreas, and intestines are impaired, and normal bowel movements become sluggish. Absorption from the gastrointestinal tract is generally diminished.

Changes also occur in the psychologic states of old people. Perceptions are not as keen as in the young. Concentration is impaired and association retarded. Retention and memory are somewhat defective. Mood is irritable, and emotional response is at times inadequate. Judgment is apt to be defective and is likely to be colored by prejudice, resentment, and suspicion. Mental tension is lowered, and there is difficulty in changing quickly from one subject to another. Less objectivity is used in reality testing and in meeting situations adequately and realistically. It is not easy for them to acquire patterns of reaction based upon current social, economic, and political views. . . .

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(*NY State J Med* 1951; 51:2370-2375)

The elderly and medicolegal trends in consent to treatment

J. RICHARD CICCONE, MD

Laws and regulations are increasingly reshaping the doctor-patient relationship, by changing it from one of covenant to one of contract. It has been observed that we are moving from informal standards of professional ethics (broad and general principles developed over centuries) to a civilly enforced body of law and administrative regulation which will change and control the doctor-patient relationship. It has not been demonstrated that this revamping of the doctor-patient relationship, in the name of protecting "patient rights" and patient autonomy, serves either societal or individual good. The medical care of the elderly has not escaped these attempts to codify and "bureaucratize" the doctor-patient relationship.[1] This paper explores recent medicolegal trends affecting medical treatment decision making for the incompetent elderly patient.

CONSENT: THE POWER TO ACCEPT OR REJECT MEDICAL TREATMENT

Competence is the cornerstone of the patient's legal right to consent to or to reject medical treatment. In 1914, Judge Cardozo wrote the often quoted words, "Every human being of adult years of sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable in damages . . . this is true except in a case of an emergency where the patient is unconscious, and where it is necessary to operate before consent can be obtained." [2] The legal doctrine of consent to treatment has undergone change in the direction of further supporting patient autonomy and reorganizing the doctor-patient relationship to make it more egalitarian. An adult is presumed to be competent to consent to treatment or to refuse treatment until a judicial finding of incompetence, based on clear and convincing evidence.

When a physician, usually a psychiatrist, is asked to evaluate a patient's competence, two points must be kept in mind. First, the physician provides a determination of clinical competence, and an opinion regarding legal competence; the physician's opinion regarding legal competence is not legally binding. Second, the physician must begin by determining who is requesting the consultation and for what purpose.[3] The question to be answered is not, "Is this patient competent?" but, "Is this patient competent for a specific task?"

The next step is to determine the presence and nature of any psychiatric illness. If a psychiatric illness is present, do the signs and symptoms impair the person's capacity to make the decision to accept or reject treatment? Does the elderly patient's illness impair awareness of the fact that he or she is being asked to accept or reject treatment? Does the mental illness impair the elderly patient's understanding of the nature of the illness for which treatment is being recommended? Does the elderly patient understand the treatment that is being recommended and the likely side effects of this treatment? Does the elderly patient understand that other treatments are available, including no treatment, and the implications of rejecting the doctor's recommendation?

Competence is not always clearly present or clearly absent. Competence may fluctuate according to a person's environment and according to the complexity of the decision that faces the elderly individual. The mildly demented may be competent to decide simple questions or to consent to nonrisky procedures but may have more difficulty when the issues are more complex.

If the elderly individual's clinical incompetence is due to a treatable illness, he or she may be restored to competence. Therefore, the physician must carefully consider the differential diagnosis of incompetence that includes an acute psychotic episode, delirium, and major depression. The specific treatment will be dictated by the specific illness or underlying cause of the clinical incompetence. The presence of a full-blown psychosis is not necessary to find incompetency. For example, the nonpsychotically depressed may be seriously impaired by negativistic thinking.

In the situation where the person is rapidly fluctuating from what appears to be a competent to an apparently incompetent state, for all practical purposes the patient is incompetent. The patient who is incompetent for days, has a "lucid interval," and then returns to a state of being incompetent is also usually considered incompetent.

WHEN THE PATIENT IS CLINICALLY INCOMPETENT

Traditionally, when an elderly patient was clinically incompetent, the physician along with the patient's family

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members could make decisions about what treatment would be given or withheld. This custom has no formal standing in law. In fact, it could lead to significant legal difficulties. What the law currently calls for is documented informed consent before medical treatment can be initiated or withdrawn.

A patient is considered legally competent until someone raises the question. Then, and only then, is the issue joined. In a social climate that emphasizes autonomy, those who are charged with responsibility for risk management often advise that formal procedures be followed in an attempt to avoid liability and malpractice suits. In New York State, in nonemergency situations where the elderly patient's capacity to care for himself or herself is questioned, the law currently provides for three procedures: durable power of attorney; conservatorship; and committee of the person. Only the durable power of attorney and the committee of the person provide the legal standing to make decisions on behalf of the incompetent individual to accept or reject treatment.

Durable Power of Attorney. The statute on durable power of attorney in New York State does not speak to health issues. A durable power of attorney is a power of attorney instituted prior to an individual's becoming incompetent which contains a specific section allowing for a continuation of the power of attorney should the person become incompetent. The New York State attorney general, however, has issued an opinion that a durable power of attorney may be used, under defined circumstances, to permit an agent to communicate the patient's decision regarding medical treatment. The durable power of attorney must state that the patient authorizes the agent to communicate these decisions.[4 (p67)]

Conservatorship in New York State. Under New York State law, adults are presumed to be competent for whatever contractual and other decisions are necessary to function in our society. Article 77 of the Mental Hygiene Law provides for the creation of a conservatorship, a mechanism to insure the financial and personal well-being of an individual, and does not require that the person be found incompetent. A petition may be filed by a relative or a friend; the meaning of friend includes corporate bodies, public agencies, or social service officials. If the proposed conservatee is in an institution, the officer in charge of the institution may also file a petition. The petition must contain the reasons for concern about the individual's well-being, the facts demonstrating the need for appointment of a conservator, and the plan the petitioner proposes to "insure the preservation, maintenance, and care of the proposed conservatee's income, assets, and personal well-being, including the provision of necessary personal, and social protective services to the conservatee." [5] When the proposed conservatee is unable to attend a hearing, a guardian ad litem must be appointed unless the court believes that the proposed conservatee's interests are adequately protected by the Mental Health Information Service or by "counsel chosen by the proposed conservatee." Jury trial is available when any party contests the need for appointment of a conservator. Usually a family member is appointed the conservator, but a nonfamily member may also be appointed, especially when there are family disagreements. In the case of *Matter of Lyon*,[6] an 84-year-old quadriplegic confined to a nursing home had a trust which could be invaded for her medical care. Her son was not appointed conservator since at issue was the extensive and expensive care that was keeping Mrs Lyon alive. The court felt that it was clear that the son considered her present care to be "squandering" in view of her condition. However, in the opinion of Mrs Lyon's physician, this care had been life saving. Family members may not always have the best interests of the conservatee in mind—particularly when they stand to inherit the estate that remains after the expense incurred by the conservatee.

Where there is no family member available, and that is not a rare event in our society, the courts have appointed nonprofit corporations as conservator. It is also possible for the Department of Social Services to act as a conservator, even if the conservatee does not receive public assistance.

A conservatorship, while charging the conservator with looking after the person and supplying his or her needs, does not empower the conservator with the legal decision making capacity regarding consent to treatment; that requires a committee of the person.

Committee of the Person. Article 78 of the Mental Hygiene Law outlines the jurisdiction, procedure, and purpose for forming a committee of the person and/or of the property. The declaration of incompetence and the appointment of a committee, more far-reaching than the formation of a conservatorship, is more difficult to accomplish because the court is reluctant to take from a person his civil rights, particularly the right to manage his own affairs. The law requires the person bringing the petition to state the facts showing incompetence and to demonstrate why a conservatorship would be inappropriate. When any party disputes the need for a committee, a jury trial is available and the burden of proof falls on the petitioner.

The committee, when appointed, is subject to the control of the court and is accountable to it. Section 15 of Article 78 reads, "the committee of the person is charged with the responsibility for taking care of the physical needs of the incompetent, furnishing him with such medical and other care as is required, and looking after his health and general welfare."

Emergency Care

In a medical emergency where the person is unconscious or clinically incompetent, treatment may be given under a theory of presumed intent. The Social Services Law §473A provides for a short-term involuntary protective services order (STIPSO).[7] A social service official can act as a petitioner in a special proceeding in the state supreme court in New York City or in a county court elsewhere in the state. The official can bring information to the court which demonstrates that the allegedly endangered adult, as a result of a lack of capacity to understand the situation, is in a life threatening situation or poses imminent risk of serious physical harm to himself or to others. The petitioner is also required to provide a description of the specific protective services needed to remedy that situation. The STIPSO emergency order is limited to 72 hours, with one renewal for 72 hours. It can be instituted simultaneously with a petition for a conservatorship or

committeeship or civil commitment for involuntary hospitalization under the Mental Hygiene Law.

The Ultimate Decision: Do Not Resuscitate (DNR)

In April 1984, the *New England Journal of Medicine* published "The physician's responsibility toward hopelessly ill patients." [8] This paper examined the physician's role in the treatment of the terminally ill adult and the writing of "do not resuscitate" orders. In spite of the importance of the patient's right to make decisions about his or her medical treatment, the authors pointed out that disease, pain, drugs, and a variety of conditions altering the patient's mental state may "severely reduce the patient's capacity for judgment." Therefore, the evaluation of the individual's competence is important in deciding to what degree to follow the patient's stated wishes. If the patient's capacity to make decisions is impaired, the physician has to turn to the patient's family and friends. A surrogate may assist by speaking on behalf of a patient. Where the physician does not have a longstanding relationship with the patient, it may be of special importance to have other means of determining the terminally ill patient's desires. A written statement, "The Living Will," may provide important but not binding evidence of the patient's wishes.

A living will is a written expression of the patient's wish to refuse treatment. Courts consider the living will persuasive evidence of the incompetent person's intention and give great weight to it in the substitutive judgment process. Those in favor of writing the living will into law maintain that: (1) it clarifies the law for both physicians and patients; (2) it allows the patient a stronger role in expressing his or her wishes; (3) it increases a physician's protection from liability—the physician is liable only if he or she fails to act in good faith, that is, he or she deliberately and intentionally acts with malice; and (4) it provides direction for the physician who cannot for any reason comply with the dying patient's written directive—the physician is directed to transfer the patient to another physician who is able to comply.[4 (pp29-30)]

Even with written documents or spoken wishes, there is no ignoring the physician's central role in the decision making process. Through education and experience, physicians have the capacity to diagnose, recommend treatment, and accept responsibility for their recommendations. Part of the physician's training has been to value life. With modern technology, this life prolonging activity may go on for long periods of time and be fueled by reports of the rare patient who recovered from a similar problem. Also encouraging inappropriate heroic measures is the tendency of physicians, at times, to equate the patient's death with his or her own inadequacy. Here, as in other circumstances, personal motivation must be examined and therapeutic ambition avoided. Defensive medicine encouraging inappropriate heroic measures is often practiced in the hopes of avoiding legal liability. An important obstacle to providing humane care and adequate treatment for the elderly is current concerns about cost containment. The push to not "squander" valuable resources on consumers who are about to die anyway may lead to inappropriate use of DNR orders. The physician must remain mindful of his or her responsibility to pursue the patient's best interests, which may not be the patient's stated choice or opinion. In addition, the physician's determination of the patient's best interest may not be simply the physician's idiosyncratic opinion, but must be based on a professionally developed code or value system which the physician applies to the specific patient.

Many hospitals have established guidelines for "do not resuscitate" policies. Where the patient is competent, these guidelines call for DNR decisions to be made by the patient. If the patient is not competent, the guidelines call for the decision to be reached by consultation with family members or legal guardians. If no patient representative is available, then the guidelines call for the courts to be approached. Any significant improvement in the patient's condition voids the DNR order and the order can be rescinded at any time by any person who contributed to the making of the decision.

Two New York State cases on the care of the terminally ill are of special note. In the case of *In re Eichner*,[9] Brother Fox, an 83-year-old member of the Society of Mary, went into a coma after surgery and was left in a permanent vegetative state. His superior, Father Eichner, petitioned the court to authorize removal of Brother Fox's respirator, on the basis of Brother Fox's previously expressed views on care of the terminally ill. The New York Court of Appeals ruled that artificial life support may be withdrawn or withheld from an incompetent patient for whom there is no reasonable chance of recovery, when there is clear and convincing evidence of the patient's wishes. There is no requirement that a person accept every available treatment. The court added that evidence of the patient's wishes need not be written; "clear and convincing" reports of conversations between the patient and family members would qualify. No civil or criminal liability would be incurred by the medical person carrying out those wishes, and prior court approval is not necessary. Court approval might be sought at the option of the treating medical team.

The case of *In re Storar*[10] involved a 52-year-old profoundly retarded, institutionalized man who was terminally ill with bladder cancer. His mother, his legal guardian, initially consented and then revoked her consent to his receiving blood transfusions on the grounds that it would only prolong his agony. Viewing blood transfusion as not being an extraordinary treatment, the New York Court of Appeals ruled that, in the absence of clearly stated evidence of the patient's wishes, a family member or guardian did not have the power to refuse treatment on the patient's behalf. Since the patient in this case had never been able to make an informed decision, there was no evidence of what his wishes would have been. Therefore, he could be provided with unwanted treatment over his guardian's objection.

Conclusion

The legal activism of the 1960s and 1970s appears to be receding in the 1980s in the face of judicial restraint and respect for clinical reality. The Supreme Court in *Youngberg v Romeo*[11] wrote that in determining whether a reasonable standard of care has been met, courts must defer to the judgment exercised by the qualified professional, who is presumed to have acted appropriately.

In New York State, the Governor's Task Force on Life and the Law has been considering the questions of the determination of death, the living will, and DNR regulations. The recommendations of this task force may be helpful or may lead to more intrusive laws and burdensome regulations which, rather than ameliorating the problem, may worsen it.

Current laws and regulations on providing treatment to the clinically incompetent adult who refuses treatment are causing problems in nursing homes. One nursing home had the experience of having one of its respected nurses reported to the "hotline" for suspected patient abuse. An elderly patient was suffering from major depression and, with the consent of the family, was given antidepressant medication against her will. An aide saw the patient being given the medication over her objection and made the call to the hotline. The Department of Health investigated the nursing home for this. The nurse was following the nursing home's clinically based policy, and she recognized the reality that not to give treatment in this instance might be more "abusive" than to provide that treatment over the patient's objection. The policy has a long history and is valued because it is streamlined and workable, and because it distinguishes between important and trivial treatment. The nurse, after making a reasonable effort to obtain the elderly patient's agreement to taking the antidepressant medication, informed the physician, who evaluated the patient's clinical competence and requested a psychiatric consultation. The patient was found to be clinically incompetent. In conjunction with the family, the physician decided what the important treatments were and directed that they be given.

Most health care facilities have followed these steps as a matter of custom. The law should endorse this custom, without adding cumbersome and wasteful steps, and remove the spectre of liability for physicians who act in good faith. What is needed is not more intrusive laws and regulations but clear professional standards to which physicians may be held accountable.*

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* Since the presentation of this paper, the California Medical Association and the Los Angeles County Medical Association have endorsed guidelines that call for an incompetent patient's family or close friends to be involved in treatment decisions.

FROM THE LIBRARY

OLD AGE

A century and a half ago, Horace Walpole wrote these lines: "About the time, or a little later, I die, the secret will be found of how to live forever." Feeling that enough time had passed to vouchsafe a reply, Helen Bevington answered:

Horace, be comforted to die.
One century has meandered by
And half the next since, it was true,
The temporal state eluded you.
Now as I read your pensive letter,
I wish myself that times were better
And I might boast how men contrive,
As you foretold, to stay alive.
By now we should possess the key
To fleshly immortality
And, if we wanted to, endeavor
To live forever and forever.
This, to my infinite regret,
Is not a custom with us yet.
I write you Horace for good cheer
Life is about as usual here.

Unfortunately, life *is* about as usual here so far as our knowledge of the nature of the aging process is concerned. But we are now standing where the stream divides. For generations we have followed the branch of infectious diseases. It has dwindled in size, but we have not yet really started the exploration of that other stream that flows in the direction of the chronic diseases of adult life and geriatrics. . . . As a result of our success in conquering infections . . . we now have an adult population that is proportionately larger than it has ever been before. It promises to grow even greater as the years roll by. This poses new problems for medicine, and hitherto neglected diseases assume compelling importance. . . . The care of the aged must not be left to the old man with the long white beard and the scythe. The time has come when we must begin to think about this problem and focus upon it that highest attribute of human intelligence, the ability to anticipate and plan for things to come. . . .

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(*NY State J Med* 1949; 49:1929–1933)

A historical overview of the recognition of appendicitis—Part II*

DALE C. SMITH, PHD

In June 1886 in Washington, DC, a new medical organization calling itself the Association of American Physicians (AAP) met for the first time. The goals of the group of 58 men were diverse, but chief among them was to bring the clinical and medical sciences together in discussions of current research issues.[1] Reginald Heber Fitz addressed the meeting on the subject of perforation of the appendix, presenting a paper which became a classic and which helped set a pattern for the relationship of medicine, surgery, and pathology for years to come.

Fitz was a graduate of Harvard Medical School who had studied pathology in Germany with Rudolph Virchow and Julius Cohnheim. He was one of the leaders of the new scientific approach to medicine in late 19th century America, and was deeply interested in the application of medical science to practice.[2] In his 1886 paper on appendicitis Fitz noted that even the most recent authorities were not agreed on the relationship of the caecum and the appendix in perityphlitis and peritonitis. With improvements being made in surgical treatment, however, it was vital to resolve the problem, since the surgeon needed to operate as early as possible and the physician had to know when to call the surgeon. Fitz explained the problems in the clinical investigation of the disease before 1886:

> The clinician obviously recognizes, as of the chiefest importance, the parts to which local treatment may be directly applied. His attention is thus conspicuously directed to the caecum, which may be evacuated, or to the perityphlitic abscess, which may be emptied. The pathologist looks for the seat and the cause of the disease, and finds that in most fatal cases of typhlitis the caecum is intact, while the appendix is ulcerated and perforated. He sees that the so-called perityphlitic abscess is usually an encysted peritonitis.

Fitz went on to suggest that the wide variety of abdominal diseases—typhlitis, perityphlitis, paratyphlitis, etc—which had created diagnostic and therapeutic confusion for half a century were all found at autopsy to be various manifestations of perforation of the appendix. The vast array of symptoms was in part explained by the widely varying positions the appendix could assume in the adult. To describe the condition Fitz coined the term appendicitis.[3]

As a pathologist Fitz recognized that there was considerable diagnostic and pathologic confusion surrounding the terms used to describe abdominal inflammations. He collected the clinical and necropsy records of 257 cases of "perforating inflammation of the appendix" in the hope of defining its essential characteristics and so improving diagnostic precision. Fitz wanted to know how to recognize perforation so that it could be managed surgically at the earliest opportunity. He knew the history of success in the surgical management of perityphlitic abscesses and he knew of the calls in the mid-1880s for surgical treatment of peritonitis. He wrote,

> [When] peritonitis becomes general, death has heretofore been almost inevitable. It is thus obvious that if laparotomy was successful in two out of three cases where a secondary general peritonitis was present, there is more than a chance of recovery by its use even in hitherto necessarily fatal cases, but it should be employed only when suitable, and not as a last resort when patients are moribund.[3]

Fitz also compared the "essential features" of fatal perforated appendix to 209 clinical reports of "cases of typhlitis and perityphlitis." From this comparison, essentially using the numerical method of Pierre Louis, Fitz concluded that perforation of the appendix was common and could explain almost all symptoms in virtually every case reported as typhlitis, perityphlitis, etc.

Fitz did not deny the possibility of other diseases; on the contrary, he specifically acknowledged the wide differential diagnosis faced when a patient presented with acute abdominal pain. For Fitz, the essential triad of symptoms indicating appendicitis included sudden, localized pain; fever; and a circumscribed swelling. He wrote, "An appreciation of the previous history of the patient [multiple attacks of appendicular inflammation were of "marked importance in aiding diagnosis"], the seat and character of the pain, the period of occurrence of the fever, and the date of the appearance of the tumor are necessary for an eliminative diagnosis."

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The views contained in this article are those of the author and should not be construed as official or as reflecting the views of the Department of Defense or the Uniformed Services University of the Health Sciences.

Included in the differential diagnosis was "inflammation of the caecum or typhlitis in an exact sense." Such inflammations did not represent cases of primary perforation; reports of such were in fact "secondary perforation of the caecum from without;" in these cases the pain was slight and protracted, fever was absent or "of late occurrence," and the "tumor is present at the beginning as a distinct nodular or doughy mass." However, "it is unnecessary to say that from a stereoral caecitis may arise a perforative appendicitis which may end in perforation. Many of the so-called cases of typhlitis terminating in resolution, associated with fecal retention and persisting after the removal of the feces, are undoubtedly of this nature." Also included in the differential diagnosis were intestinal obstruction, pelvic peritonitis of gynecological origin, psoitis, renal or biliary colic, movable kidney, caries of the spine or hip joint, suppurative nephritis, intestinal tuberculosis, and cancer of the cecum.[3] All of these afflictions were already being addressed by surgeons in the 1880s.[4]

Dr Fitz addressed the issue of the treatment of appendicitis in a straightforward way:

> The possibility of a termination by resolution must be recognized, and the earliest therapeutic efforts should have this result in view; especially as these efforts also tend toward localizing the peritonitis . . . To keep the bowels quiet should be the first and last thought. Absolute rest in bed, liquid diet in small quantities often repeated, and above all, sufficient opium to neutralize pain . . . If after the first twenty four hours from the onset of severe pain, the peritonitis is evidently spreading, and the condition of the patient is grave, the question should be entertained of an immediate operation for exposing the appendix and determining its condition with reference to its removal. If any good result is to arise from such treatment, it must be applied early.
>
> If surgical interference is not instituted within the first twenty four hours after the onset of the sudden and intense right iliac pain, to keep the bowels quiet must still be the injunction. The formation of the tumor, the circumscribing of the peritonitis, is then to be awaited. It is sure to form, in the large majority of cases, if the patient lives long enough.[3]

According to Fitz, the abscess that formed was then to be drained following the Willard Parker tradition. In cases of perforation of the inflamed appendix, where peritonitis would sooner or later be a consideration, early operation was clearly the treatment of choice. This was particularly true since the dramatic progress in surgery over the preceding 20 years (since the papers of Parker and Lister) had shifted the relative risk. In 1867 surgery had increased the risk to the patient; in 1886 Fitz believed it reduced the risk.

Fitz was pioneering new ground—the relationship of emerging specialists in internal medicine and surgery and the dependence of both on the science of the pathologists—but he clearly saw the importance of the relationship and did his best to help his colleagues in the medical profession appreciate the change that was occurring in medical practice. Fitz described a "borderland of medicine and surgery" which was "ever changing and surrounding a territory open to each, productive to all." He called on physicians to recognize when they had reached the limits of diagnostic ability or therapeutic effectiveness and to surrender the patient to the surgeon before it was too late. But he also cautioned surgeons to have greater familiarity with pathology, to follow the subsequent history of the patient, and to be sure the operation in fact relieved the condition it was intended to relieve.[5]

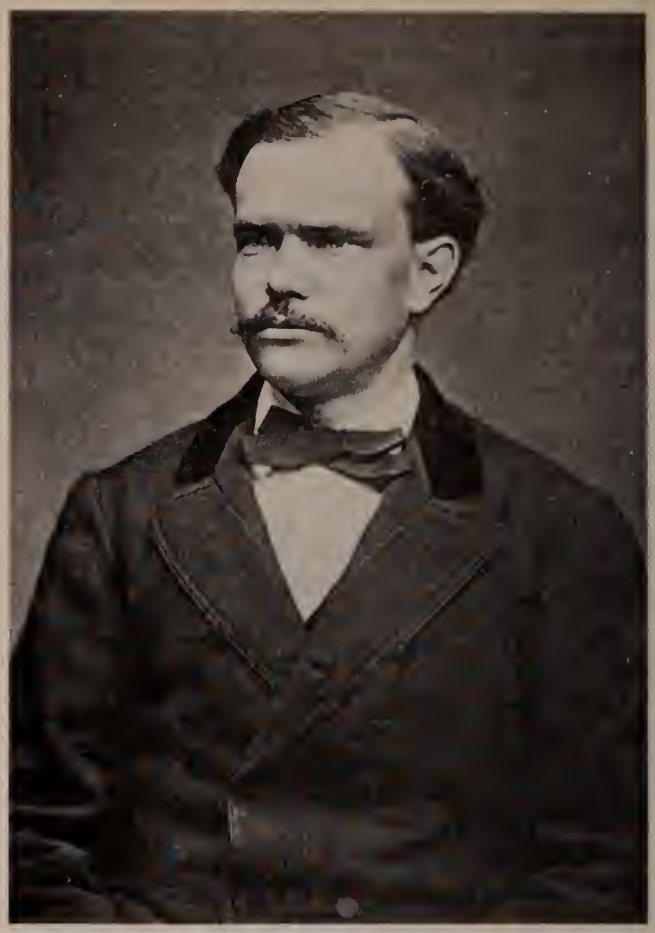

FIGURE 1. Reginald Heber Fitz, MD (1843–1913). Author of the classic 1886 paper in which the term appendicitis was introduced.

That such cooperation was possible and productive in 19th century America is illustrated by the first known case of diagnosed appendicitis relieved by appendectomy following Fitz's paper.* On April 20, 1887, a 26-year-old man consulted Dr Frank Woodbury of Philadelphia, complaining of a sudden and severe attack of abdominal pain which had prostrated him the previous day. With the passage of time the patient grew steadily worse. The abdominal pain increased, and a point of great tenderness was located approximately midway between the umbilicus and the mid-part of the Poupart's ligament. Dr Woodbury called in Dr James C. Wilson for consultation and the two physicians agreed that the man seemed to be suffering from perityphlitis. Dr Thomas G. Morton was called in for surgical consultation to consider the advisability of an operation. He advised immediate operation, and on incision found an abscess containing an ulcerated appendix and a fecal concretion. The appendix was ligated with silk near the cecum and removed together with a portion of affected

* Richard Hall, frequently credited with the first successful appendectomy, is not discussed because the operation was an accidental result of a misdiagnosis. As Hall's[6] paper made clear and Henry Sands[7] later commented, the appendectomy occurred "during an operation for a supposed strangulated hernia, the hernial sac was found to contain an appendix vermiformis which was the seat of a perforation caused by tubercular disease." Since Hall did not initially claim, and his contemporaries did not acknowledge, any particular priority, it seems inappropriate to do so in retrospect.

FIGURE 2. Frank Woodbury, MD (1848–1927) (left), the physician who in April 1887 called in Thomas Morton, MD (1835–1903) (right) to perform the first successful operation for removal of a preoperatively diagnosed perforated appendix. (Woodbury's portrait is taken from Irving Watson's *Physicians and Surgeons of the United States*, Concord, NH, Republican Press Association, 1896.)

omentum. The abdominal cavity was rinsed until clear and the wound was closed with a drainage tube extending to the lowest portion of the pelvic basin. The patient recovered without complications.[8]

Diagnosis and the Probability of Perforation

However, Morton's case, like Fitz's pathologic evidence, left important clinical problems unresolved. In the conclusion of his paper, based on a study of clinical notes and postmortem reports of perforation of the appendix, Fitz had said, "its diagnosis, in most cases, is comparatively easy." But Fitz was a pathologist; he had only received a hospital appointment in the medical service of Massachusetts General Hospital in 1886, and his clinical experience was very limited. In the discussion that followed the presentation of Fitz's paper at the June 1886 AAP meeting, Dr William Pepper rose to describe two cases, commenting, "I have mentioned these two cases because they serve to emphasize . . . the difficulty of diagnosis of this affection in its early stage." Dr Pepper was Professor of Medicine at the University of Pennsylvania, and had extensive clinical and pathological experience with the disease (having published on it at least four times). In some measure Pepper may have missed Fitz's point about the frequency of occurrence of appendiceal perforations, but he may also not have been fully convinced by Fitz's numerical approach that all cases could ultimately be resolved surgically. Pepper concluded:

> As to the difficulty of diagnosis . . . perforative appendicitis presents a marked contrast to typhlitis and perityphlitis, in which fullness or tumor in the right iliac fossa is vastly more common. This is most important because operative interference which gives the only chance of saving life in perforative appendicitis is indicated at a much earlier period than in other affections.

Fitz had allowed the possibility that there were abscesses described as perityphlitic which were not the result of perforation of the appendix, and he clearly understood that not all appendicitis resulted in perforation. His postmortem group of 257 cases was selected on the basis of perforation of the appendix. Despite his efforts to clarify the issue, however, the pathology was not clear; like Virchow, he distinguished paratyphlitis and perityphlitis by the tissue that was inflamed:

> In a like manner the rare, primary, perforating typhlitis [cecal perforation] may be followed by a perityphlitis—that is, an encysted peritonitis about the caecum, or by a paratyphlitis. The perityphlitic abscess of the surgeon, when seen early, is thus usually an encysted peritonitis of appendicular origin. More rarely, at this date, it may be the result of a suppurative paratyphlitis. The causes of this last affection are numerous and by no means

confined to the appendix or caecum, although a perforating inflammation of each of these parts of the intestinal tract may act as a cause.

He *believed* that most of the clinical cases were of the same etiology.

As a circumscribed peritonitis is simply one event, although usually the most important, in the history of inflammation of the appendix, it seems preferable to use the term appendicitis to express the primary condition. This may terminate as an appendicular peritonitis or as a paratyphlitis.

The clinicians at the AAP meeting clearly wanted to know which condition was the cause of a particular patient's pain. Most believed, with Pepper, that perforation was a surgical problem but that what Fitz had called suppurative paratyphlitis—inflammation without perforation—was to be medically managed and drained using the Willard Parker operation if an abscess formed. But Alfred Loomis of New York City did not believe you could tell one condition from another antemortem. "It has seemed to me from my own experience that it is impossible by the ordinary methods of examination to reach an early diagnosis in the majority of these cases." Even more difficult was the problem posed by Edward Janeway of Bellevue Hospital: "The difficulty is to distinguish between those cases in which we are going to have a localized peritonitis and those in which there is simply a cellular tissue inflammation."

Fitz, in closing, acknowledged the reality of these clinical difficulties: "So impressed have I been with the obscurity of the signs of incipient inflammation of the appendix that no attempt has been made to consider the process until there was evidence that perforation had taken place."[3] In that acknowledgment we see again the importance of Mikulicz's agenda—the recognition that early surgical therapy was the only valid approach to the treatment of perforation.

The wider medical community responded variously to Fitz's ideas regarding the frequency of inflammation of the appendix and the appropriate therapy. Some simply ignored the new research, such as Nathan Smith Davis,[9] who as a professor of medicine lectured on perityphlitis on December 2, 1887. His account could easily have been written 20 years before. According to Davis, operative interference was only to be considered as a last resort, when the patient was clearly dying and all therapeutic efforts had failed. Then, he said, "I would regard laparotomy as a justifiable procedure and would not hesitate to perform the operation. The patient can only die. . . ." Nathan Smith Davis reflected the past; he saw little role for surgery and none at all for surgeons.

For the community of practitioners who were well trained and widely read, like Woodbury and Morton, the application of Fitz's ideas was appropriate in clearcut cases of perforation of the appendix with spreading peritonitis. But the broader implications of appendicitis as an essentially surgical problem, though clear in retrospect, were by no means obvious, even to Fitz, in 1886.

Henry Sands was unimpressed by Fitz's theoretical disease, appendicitis, although he clearly believed that the appendix was the source of trouble in the vast majority of cases. Clinically he was more comfortable with four classes of disease—inflammatory tumors that resolved, circumscribed abscesses, acute peritonitis, and subacute or obscure peritonitis. The inflammatory tumors were, he felt, most common and should be medically managed. The two forms of peritonitis were to be operated on by laparotomy as soon as possible. But circumscribed abscesses suggested delay; Sands held that these abscesses were extraperitoneal and so the Parker operation was less dangerous than laparotomy. Late laparotomy had a strong potential for producing general peritonitis while early laparotomy was even more risky; and it was impossible to perform the Parker operation early. Sands believed that the risk of waiting was drastically overstated by proponents of early operation in cases of perityphlitic abscess.

On December 30, 1887, Dr Sands was called in for consultation on a case of "acute septic peritonitis, caused by perforation of the vermiform appendix." He advised immediate laparotomy, but the family would not consent without obtaining another surgical opinion. Dr William Bull was sent for and he concurred that surgery was indicated. Bull, however, preferred a more conservative approach, as if for perityphlitic abscess, with the incision to be extended only if it were found necessary to enter the peritoneal cavity. Sands[7] successfully held out for laparotomy, and found a ruptured appendix which he closed with three uninterrupted silk sutures. He washed the cavity and the patient recovered. The case provided Sands with the success he had been seeking and, more importantly, with a solid clinical foundation from which to dispute with Fitz. This he did in a presentation before the New York Surgical Society on February 8, 1888.

Sands realized he had an uphill fight; Fitz's use of the numerical method was an approach to medical research widely accepted in America by the 1880s.[10] While Sands did not question the validity of the numerical method, he did show the clinician's skepticism toward the research scientist with no clinical experience. Sands[7] believed that Fitz, who had no surgical experience, fell "into the easy error of putting under the same heading things so essentially different from one another that they are entirely unfit for purposes of comparison."

Fitz[11] responded to Sands' presentation with a second paper examining in greater detail the relationship of perforation of the appendix to perityphlitic abscesses. He noted that in the reports of surgeons and pathologists, the abscesses found in the first week of the disease were intraperitoneal. The extraperitoneal appearance observed by Sands and other surgeons was a result of the fact that "the walls of the abscess are formed by adhesions between the parietal and the visceral peritoneum." Surgeons were, according to Fitz, observing through a two-inch incision, pathologists through a "Y" incision. Fitz believed his pathologic evidence was more convincing.

In contrast to many practitioners in 1888, both Sands and Fitz were in agreement that disease of the appendix, whether representing one pathological condition or four clinical entities, was essentially a matter for surgical treatment. Fitz[11]: " . . . in the light of our present knowledge, the surgical treatment of this lesion offers the best chances for the life and future health of the patient, and . . . the progress of the disease needs to be watched with

knife in hand." Sands[7]: " . . . all the diseases to which I have referred are surgical cases from their beginning, and . . . surgeons alone are competent to decide whether operations are expedient, and to perform them, when necessary, at the right-time and in the right manner."

As Fitz was refining his concept of appendicitis in response to the discussion following his 1886 paper and in response to Henry Sands' 1888 presentation, the medical community of the nation was grappling with the issues he had raised. Three different communities with rich medical traditions—Boston, Cincinnati, and Philadelphia—dealt with the issue in some form in 1887.

The Dissemination of Fitz's Work

At the February 2, 1887, meeting of the Surgical Section of the Suffolk District Medical Society, David Cheever,[12] Professor of Surgery at Harvard Medical School, read a paper on surgery of the abdomen. He described eight cases in which he had operated; two are of interest for the diagnostic terms he chose. The first case he described as a pericecal abscess which was treated by three abdominal incisions, "one in the median line, and one at each side of it." There was a large cavity of pus but "no connection with the viscera was detected and the intestines were apparently walled off by inflammatory exudation." Six weeks after surgery, the left lateral incision developed a fecal discharge which healed spontaneously. Dr Cheever thought the etiology was a "low or tubercular ulceration of the bowel. The original site of the abscess was near the caecum . . . ." The second case "was probably a case of perityphlitic abscess finally descending into the pelvis." The abscess was successfully drained. In neither case report was the vermiform appendix mentioned.

In discussion, J. Collins Warren called the attention of the meeting to Fitz's recent publication and described a case seen in December 1886 in which he had asked Fitz to see the patient in consultation before operating.[13] More significant was the discussion by George B. Shattuck, a physician at Boston City Hospital where Cheever was a surgeon. In 1883 Shattuck's house officer had reported, as part of a series of cases seen on the medical service, a fatal case of perityphlitis. There was no indication of consultation.[14] Shattuck mentioned two cases recently seen on his medical service by Cheever, who decided not to operate; one patient recovered under medical management, one died of tuberculosis of a fallopian tube which produced fatal peritonitis. For Shattuck in early 1887, surgical treatment was not always advisable "but the advisability should be carefully weighed before collapse rendered the operation desperate if undertaken."[13]

In Boston, early in 1887, Fitz was beginning to be considered but did not yet seem to have had much impact. The cooperative framework of physician and surgeon consulting about the acute abdomen had already been established among the best practitioners of the city. Warren's example suggested that Fitz's work on "pus in the neighborhood of the appendix vermiformis" would be integrated into this framework but not in as yet obvious ways.

At the June 6, 1887, meeting of the Academy of Medicine in Cincinnati, Dr Cleveland reported a case of perityphlitis in an infant followed by erysipelis. The surgical citations were to William Bull (1873) and Henry Sands (1880) on the disease and to Lawson Tait on laparotomy. The community was evidently a widely read one for there was discussion of the bacterial cause of erysipelis and of Moritz Kaposis' recent questions concerning the work of Koch and Fehling. Once more the actual case predated Fitz's publication and the issues were abscess and surgical infection so Fitz was not as obviously germane.[15]

Finally, in Philadelphia, the county medical society devoted its December 14, 1887, meeting to a consideration of pericecal inflammations. There were three invited papers followed by general discussion; the first paper was by J. H. Musser[16] on pathology. Musser was followed by William Pepper[17] on diagnosis and by Thomas G. Morton[18] on treatment. Musser took a middle ground between the past and the future, choosing to use all the old terms and Fitz's new term—appendicitis.

Musser suggested a pathology in which two tracks of disease lead to the same clinical manifestation. Inflammation of the appendix—appendicitis—could lead to appendicular peritonitis (With's term), or "inflammation of the appendix and its serous covering"; or it could lead to "para-typhlitis or inflammation of the connective tissue around the appendix." Similarly, according to Musser, typhlitis was inflammation of the cecum; perityphlitis was "inflammation of the peritoneum covering the caecum"; and "para-typhlitis, inflammation of the connective tissue behind the caecum." He accepted Fitz's numerical analysis that perforation of the cecum was extremely rare and that most disease of the pericecal region was "due primarily to inflammation of the appendix." Musser commented on the difficulty of performing autopsies in cases of peritonitis and on the fact that many cases seemed to resolve naturally. Some cases of perforation might heal, and there was no evidence of fatal pericecal disease without the appendix being involved.[16]

William Pepper, while having no objection to Musser's terminology, argued that most practitioners were not going to change and that his paratyphilitis would continue to be called perityphlitis. Pepper stressed the number of autopsies of patients dead of other causes in which evidence of a former inflammation of the appendix was found, but where there was no history of disease; the best estimate was about one third of cases. Furthermore, he disagreed about the rarity of cecal inflammation:

> In a long experience in which I have paid much attention to these cases, I have collected a number of instances of independent caecal disease, sometimes going on to chronic inflammation, ulceration and perforation . . . there are a considerable number of cases of typhlitis where the symptoms are chiefly due to inflammation of the walls of a cecum and the peri-cecal connective tissue, which end in recovery.

Given these two classes of disease, Pepper felt that despite the value of Fitz's work on perforation of the appendix, "the record is not to be sought on the post mortem table, for the large proportion of these cases if properly treated from the beginning end in resolution." The challenge for Pepper in late 1887 remained, as it had been in June 1886, one of diagnosis, and "in particular, [to] strive to point out the indications for operation in the two classes of cases."[17]

Thomas Morton followed Pepper's line of reasoning in

his discussion of therapy. "For practical purposes the treatment of peri-caecal inflammations must be divided into two subdivisions, that of the pre-purulent and that of the post-purulent stage, or, first, before formation of pus or of appendix perforation; and, second, after that event." The first class was to be treated medically, the second surgically, but he had certain reservations leaning toward increased surgical management. "Prompt resolution should take place in cases which are not to go on to the stage of pus formation; and very long continuation of symptoms, or relapses, or recurrences, would be strong indications for surgical interference." Finally, for Morton, the pathological process was not of overriding concern: "Typhoid, caecal, or appendicular inflammation or perforation should likewise receive identical treatment as for the simple inflammatory disorders of that region."[18]

In discussion W. W. Keen called Pepper's efforts at diagnostic discrimination into question and advocated a more vigorous surgical stance than had Morton: "Exploratory operation is not only constantly done, but done, I may almost say, without any additional risk to the patient, and it gives us the means of dealing with whatever lesion we may find." But when pushed in further discussion, he withdrew slightly: "I do not wish to be understood as advocating indiscriminate laparotomy in cases of peri-caecal inflammation." Like Pepper, William Osler was also impressed by the number of cases in which patients recovered without surgery and he described three cases of pericecal abscess from disease of the cecum. Osler also called attention to the variations in anatomy in the region, stressing the importance of the relationship of any abscess to the peritoneum.[19]

The general consensus in 1887 seemed to be that laparotomy was indicated for perforation, but most clinicians held with William Pepper and Henry Sands that there was a disease of the cecum and that many such cases recovered without surgical interference. Only the pathologist Musser seemed to hold with Fitz that typhlitis was insignificant when compared in terms of frequency with appendicitis. Their common pathological orientation, however, whereby they observed disease states primarily at postmortem, is not sufficient explanation for their unique position in regard to the relative frequency of appendicitis. Osler had probably done as many postmortems as either of Fitz or Musser and he was not convinced.

At the January 1888 meeting of the Suffolk District Medical Society the members heard a paper read by Maurice H. Richardson, surgeon at Massachusetts General Hospital, and a case report by J. W. Elliot. The consensus remained unchanged: In mild, subacute, or chronic cases the expectant or medical treatment was preferred.[20] But in 1888 a new clarity would begin to emerge. It would not come from pathologists, but from surgeons doing living pathology. In particular, Charles McBurney, Nicholas Senn, and perhaps Henry Sands, would operate on cases of presumed perforation to find an unperforated but violently inflamed appendix. They would become the leaders of a new school of thought advocating early diagnosis and early laparotomy which over the next generation would result in the recognizably modern management of appendicitis.

Surgeons Take the Lead

At the May 23, 1888, meeting of the New York Surgical Society, Charles McBurney[21] presented a case of septic peritonitis resulting from appendix perforation. He reported in passing that he "had that day operated in a case in which perforation had been imminent, but had not yet taken place. The appendix, which was very tense and full of thick pus, was separated from its adhesions and removed uninjured, so that no sepsis could occur." Arped Gerster in discussion recognized the significance of McBurney's case. "Such facts as Dr. McBurney's operation had revealed would probably tend to give our operative endeavors an entirely new direction." If one could detect the diseased appendix and operate "at a time when the process was still limited to the vermiform appendix" to achieve "a safe removal of the sac and its contents," then surgery was technically easier and considerably safer.

The exact role Henry Sands played in the events of 1888 is unclear; he died in November without publishing further, but McBurney[22] recalled, "Sands devoted much attention to this study and it was my privilege to assist him in a number of successful operations for the removal of the appendix in an early stage of the disease."

Later in 1888 Nicholas Senn[23] of Chicago operated in a case in which the appendix turned out not to be perforated, again proving the existence of catarrhal appendicitis.

FIGURE 3. Charles McBurney, MD (1845–1913). Professor of Surgery at the College of Physicians and Surgeons, New York, and student and follower of Sands and Parker, who pioneered the removal of the appendix prior to perforation.

He reached the now classic conclusion: "It is of the greatest practical importance to recognize the exact condition in time, and to anticipate the dangerous and only too often fatal complication by removing permanently the source of danger, which can be done at this time with comparative ease and almost perfect safety by the extirpation of the appendix."

Before the full implications of these surgical observations could be brought to the attention of the medical world, William Bull[24] presented a paper at the September 18–20, 1888, meeting of the American Surgical Association. The clinical problems were still real: "We preach early interference, but our practice is not always early enough to save life. . . . " Why? He had all the data, he cited all the important literature reviews. Bull suggested, as had others before him, "we may distinguish by dissection between an inflammation of the caecum or its appendix, I do not think we are yet in a position to do so clinically." He still believed in a relatively benign "catarrhal perityphlitis" which was not an indication for surgical interference, so all he could urge was "the performance of the operation before the generalized peritonitis is well established." He did not even hope to operate before peritonitis occurred.

Further difficulties were made manifest in discussion as Joseph Ransohoff of Cincinnati cited a wide variety of cecal lesions that might produce right lower quadrant disease, including not just the ideopathic or catarrhal but tubercular, dysenteric, and malignant lesions as well. "Not every pericaecal inflammation is the result of perforating appendicitis." Such attitudes were seconded by other surgeons until Reginald Fitz, apparently invited to attend because of Bull's paper, made a stronger, more general statement than he had previously made. Not only was he increasingly coming "to disregard the caecum" but, he stated, "It is apparently the existence of actual inflammation on the appendix that produces the symptoms." With this sentence Fitz went beyond the conclusions from his own postmortem data to take into account the yet uncollected cases of surgically observed appendicitis before perforation. But Fitz lost his credibility with surgeons when, in response to the problem of inability to locate the appendix buried in a mass of adhesions, he thoughtlessly said:

> It seems to me that it is impossible to avoid finding the appendix. The only point to remember is that the appendix arises from the caecum . . . If the exploratory operation does not result in disclosing the appendix, it is not sufficiently thorough . . . the object of the exploration should be the discovery of the appendix.

In his quiet conclusion of the discussion for the surgeons Bull[24] simply pointed out that Fitz was wrong; such exploration was possible but was frequently too dangerous for the patient.

Three papers that appeared in late 1889 shaped the future and captured the attention of America's leading surgeons. Two were important only as confirmation: Senn's [23] November paper and J. B. Murphy's[25] December paper. Murphy's paper described what he believed was the first case of acute, nonperforated appendicitis cured by operation. But Charles McBurney's[22] paper, also published in December, went much further. He extended Fitz's denial of the importance of typhlitis from the autopsy suite to the

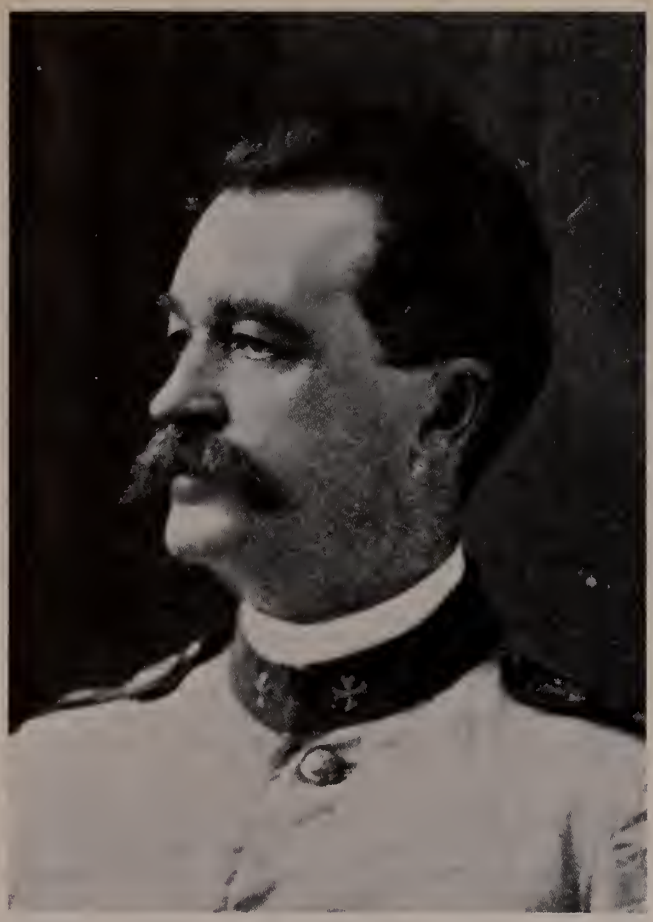

FIGURE 4. Nicholas Senn, MD (1844–1908). Midwestern surgeon and a pioneer in early laparotomy for appendicitis.

operating room: "How many cases of localized peritonitis or perityphlitis arise from impaction of feces in the cecum [the etiology of simple typhlitis] . . . . Is there a single observation brought from the dead-house or from the operating tables to suggest this idea?" Furthermore, he strongly seconded Fitz on naming the process because of its implications: "I must, therefore, prefer to use the term inflammation of the appendix or appendicitis, and give up once and for all, the terms perityphlitis, paratyphlitis, and extra peritoneal abscess, as misleading and not valuable except in explanation of secondary pathological conditions." The name had therapeutic implications; if the disease was appendicitis, then remove the appendix. For "if it can be shown by future experience with improved methods of operation and with more perfect antiseptic precautions that the exploratory incision for inspection of the diseased appendix is much more free from danger than the expectant treatment, then there could be but one answer to the question: What is the best treatment?"

McBurney did not trust symptoms as a guide—he had found them fatally flawed—but he did acknowledge that accurate diagnosis was important in the early recognition of appendicitis. Everyone agreed that pain in the right iliac region was an early sign of perityphlitis and typhlitis. McBurney provided a means of determining whether that pain meant appendicitis.

> Whatever may be the position of the healthy appendices found in the dead-house—and I am well aware that its position when in-

FIGURE 5. Charles McBurney operating at Roosevelt Hospital, New York, in 1900.

> flamed varies greatly—I have found in all of my operations that it lay, either thickened, shortened, or adherent, very close to its point of attachment to the cecum. This, of course, must, in the early stages of the disease, determine the seat of greatest pain on pressure. And I believe that in every case the seat of greatest pain, determined by the pressure of one finger, has been very exactly between an inch and a half and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus.[22]

The papers of 1889 did not resolve the issue. The timing and nature of operative treatment continued to be debated. But Senn and Murphy would win converts in the midwest, and McBurney would be joined by George R. Fowler in New York City, W. W. Keen and John Deaver in Philadelphia, as well as others around the country, and in the 1890s would lead an increasingly vigorous campaign for early operation. Fitz would be left behind, for his lack of clinical experience made him, to a great extent, a necessary follower of senior clinician/pathologists like William Pepper. J. M. T. Finney[26] told of one 1888–1889 case, for example, seen in consultation by Fitz and John Homans, in which it was Fitz who counseled delay while Homans proposed immediate surgery.

At the June 9, 1891, meeting of the Surgical Section of the Massachusetts Medical Society, the theme was the diagnosis and treatment of inflammations of the appendix. J. Collins Warren[27] introduced the subject by presenting two cases: in one case the patient had a perityphlitic abscess which ruptured in the hospital (immediate operation saved him); the second case terminated fatally despite mild symptoms. Warren was followed by 13 physicians, 11 of whom held variations of the opinions expressed by Fitz, essentially that some patients did not require surgery. Included in this group were leading surgeons like David Cheever and John Homans, leading "internists" like Frederick Shattuck, and general practitioners. In the words of Fitz, the problem remained:

> What seems to me of even greater importance than accuracy of diagnosis, so easy in general, is the question when medical treatment shall cease and surgical treatment begin. Were perforation actually present, there would be no question in my mind; but I know no diagnostic means by which one may absolutely determine at the outset whether perforation is present or absent. In doubtful cases we should wait and treat the patient medically, until we get more direct indication for surgical treatment than may be present when he is first seen.[27]

This opinion contrasted with the ideas of Alfred Worcester of Waltham, who was firmly convinced that "the right treatment . . . is to operate first, last and every time," or those of Henry Marsh, "If there is any doubt, give the patient the benefit of it, and operate."[27]

In that same year, 1891, there was a similar discussion before the Medical Society of the State of New York; but there the surgeons favoring early laparotomy were much more visible. Led by Charles McBurney, who reported 24 early operations, surgeons like Fowler and Keen presented a unified front. For Keen,[28] "The first indication is to call a surgeon"—yet another expression of the belief that acute abdominal disease was essentially a surgical issue. Physicians like Fitz, Pepper, and Osler would continue to worry through the 1890s about case differentiation, but an increasingly sharply defined group of practitioners who saw themselves as surgeons would abandon such activities as counterproductive. As early as 1888 J. McFadden Gaston,[29] an Atlanta surgeon, had recognized the trend "among surgeons":

> . . . with the uncertainty which hangs over the diagnosis in the early stage of appendicular disorder, the expectant treatment is generally recognized as the most prudent course but there is a growing tendency among surgeons to cut the Gordian knot by a decisive step, and use an exploratory operation by incision for determining the exact seat and character of the disturbance. This course is indicated when the symptoms are such as to raise a presumption in favor of appendicular inflammation, in advance of those phenomena which usually accompany perforation.

The extension of these ideas was a slow process, the business of professional reeducation. In part, it required progress in technique and achievements in asepsis (masks were only introduced at the close of the 19th century). In part it was a question of specialization—who should operate and how were they to be trained? Slowly, over the last decade of the 19th century and the early years of the 20th, progress was made. Progress would of course continue as clinical pathologists provided further diagnostic data in the 20th century. But a great stride was made 100 years ago when the pathologist Reginald H. Fitz defined a disease that had a surgical therapy and so sharpened what had been a confusing issue. He did *not* create a revolution in medical science or surgical practice; in fact, he was never fully converted to the idea of operative therapy for acute appendicitis. Surgeons facing the reality of clinical difficulties and diagnostic imprecision were every bit as or even more crucial to the evolution of modern surgery. Fitz was, however, a vital part because without his insights into the pathophysiological process of appendicitis, it is difficult to understand what shape the debate would have taken and how it would have been resolved.

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APPENDICITIS IN CHILDREN

Children's surgery differs from adult surgery in many particulars.

In the osseous system its peculiarities are so marked that children's hospitals and orthopedic hospitals are almost synonymous terms in many cities.

In the lymphatic system there are similar peculiarities, for children's lymph nodes show both suppurative and tuberculous inflammations more frequently than adults'; and the type of inflammation, too, differs with different stages of childhood, the suppurative forms being more common before the age of two years, and the tubercular forms increasing in relative frequency after that age.

The thoracic inflammations of children differ widely from those of adults.

Tubercular serous effusions are rarer. Purulent pneumococcus and streptococcus effusions are more common.

The abdomen shows peculiarities in its inflammations as marked as any of those already mentioned.

Biliary and gastric inflammations are rare. Tubercular peritonitis is more common than in adults, but the ascitic form is seldom seen.

General suppurative peritonitis from unknown cause is much more common in children, also pneumococcus peritonitis, and probably general gonococcus peritonitis.

Since children present so many surgical peculiarities, one would expect their attacks of appendicitis to show noteworthy features; and they do. . . .

The diagnosis in children is complicated by many factors. It is usually difficult or impossible to obtain a clear statement of symptoms or an accurate localization of pain, and symptoms which guide us in adults are in children frequently due to other causes than appendicitis. Hence, we hear of multiple consultations, of delays and indecision, and of progression to general peritonitis, or multiple abscesses, in the kind of cases which are promptly and successfully treated in adults. . . .

CHARLES N. DOWD, MD
(*NY State J Med* 1910; 10:100–103)

Coexistence of sarcoidosis and carcinoma in a solitary pulmonary nodule

ANGELA SAVINO, MD; PAUL D. OSTROVSKY, MD; ABRAHAM SANDERS, MD; STEPHEN M. DALY, MD

The most common manifestation of sarcoidosis is pulmonary involvement, occurring in 75–90% of patients. Bilaterally symmetric enlargement of hilar and paratracheal lymph nodes, with or without diffuse parenchymal disease, is common. Unilateral hilar adenopathy occurs in 1–3% of cases. Solitary pulmonary nodules have also been reported.[1] These nodules manifest no radiographic characteristics to suggest their histologic composition. We describe a patient with both sarcoidosis and adenocarcinoma in a solitary pulmonary nodule, the latter possibly representing a scar carcinoma.

CASE REPORT

A 44-year-old black woman was found to have a 2 cm nodule in the upper lobe of the right lung. The nodule was detected on a preoperative chest film for cosmetic surgery in 1983. Since the patient was presumed to be in excellent health, the preoperative chest radiograph was not reviewed, and the nodule was not investigated at that time. One year later, papular skin lesions developed on the patient's eyelids, face, and shoulders. Biopsies of the skin lesions revealed noncaseating granulomas, and a diagnosis of sarcoidosis was made.

Physical examination was remarkable only for the skin lesions. There was no lymphadenopathy. Laboratory studies showed normal liver and renal function. A purified protein derivative test was nonreactive, in contrast to reactivity shown a year earlier. The level of angiotensin converting enzyme was normal.

The admitting chest film, taken on June 3, 1985, revealed a nodule that had increased in size since 1983 in the anterior segment of the right upper lobe. There was new right hilar and right paratracheal adenopathy (Figs 1, 2). In addition, a computed tomographic scan showed adenopathy in the anterior and posterior mediastina. The pleura and pericardium were unremarkable.

FIGURE 1. Chest film taken in December 1983 showing a 2 cm noncalcified nodule in the right upper lobe. There is no mediastinal or hilar lymphadenopathy.

A percutaneous needle biopsy with an 18-gauge needle was performed under fluoroscopic guidance. Cytologic studies revealed no evidence of malignant cells, but multinucleated giant cells suggestive of sarcoidosis were seen. The patient underwent a right thoracotomy, at which time the pleural and pericardial surfaces were noted to be studded with tiny nodules. A wedge resection of the nodule in the right upper lobe and biopsies of pleural nodules and paratracheal nodes were done. Pathologic study revealed well-differentiated adenocarcinoma surrounded by remnants of sarcoid granulomas in the nodule. The pleural nodules were metastatic adenocarcinoma. The paratracheal nodes showed the lesions of sarcoidosis (Fig 3).

FIGURE 2. Chest film taken in June 1985 showing increased size of nodule in the right upper lobe, with linear streaks radiating to the right hilum. Right hilar and paratracheal lymphadenopathy is apparent.

DISCUSSION

Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology that affects mostly young adults. Common manifestations of the disease include bilateral hilar lymphadenopathy, pulmonary infiltration, and skin or eye lesions. It is characterized pathologically by noncaseating granulomas.

The association of sarcoidosis and malignancy is unclear. At least one large study[2] suggested that there may be an increased incidence of malignant lymphoma and lung cancer in patients with pulmonary sarcoidosis. The authors speculate that this may result from immunologic deficiencies in these patients.[2] The association of sarcoidosis and pulmonary neoplasm is an important one due to the diagnostic problems encountered when new roentgenologic

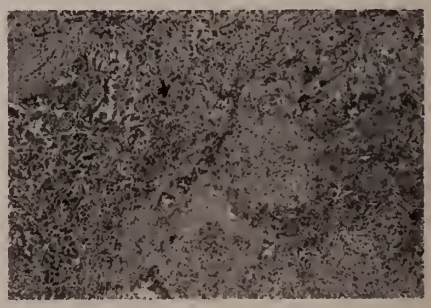

FIGURE 3. Section of lung parenchyma showing adenocarcinoma in the left half of the field (solid arrow); adjacent sarcoid granulomas are seen on the right (open arrow) (original magnification ×100).

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findings occur in these patients. Malignancy may be overlooked if these findings are attributed to the preexisting disease.

Sarcoidosis is most frequent in the third and fourth decades of life; it affects blacks ten times more frequently than Caucasians in the United States, and the incidence in women is usually double that in men. In contrast, bronchogenic carcinoma is unusual before the age of 35 and has no racial predilection.

The patient we describe had no risk factors for bronchogenic carcinoma and had active sarcoid skin lesions. The increasing size of the nodule could have been a manifestation of active pulmonary sarcoidosis. Granulomas are known to enlarge, as can be seen in patients with histoplasmosis, tuberculosis, and coccidioidomycosis.

Transbronchial biopsy is an effective means of diagnosing pulmonary sarcoidosis. The disorder can be diagnosed in up to 96% of patients in whom parenchymal disease is roentgenographically apparent, and in 44% of patients in whom it is not apparent.[3] Due to the peripheral location of the lesion in this case, percutaneous needle biopsy was performed. Benign disease can be identified in up to 88% of cases, and a specific diagnosis can be made in 68% of patients using transbronchial biopsy. However, it is emphasized in the literature that careful follow-up is essential, and repeat biopsy or surgery is necessary if nonspecific inflammation or fibrosis is found.[4]

It is of interest that on pathologic examination, the primary tumor was surrounded by remnants of sarcoid granulomas. Cancer of the lung can originate in a preexisting scar, and this scenario accounts for up to 7% of all lung tumors. These "scar cancers" are located peripherally, with no evidence of bronchial origin, and they occur around true hyalinized scar tissue. They are further characterized by thickening and puckering of the pleura overlying the tumor, deposition of anthracotic pigment, and accumulation of cholesterol crystals. In one large series, 72% of scar cancers were adenocarcinomas, 18% were squamous cell type, and the remainder were undifferentiated in type.[5]

We speculate that the carcinoma in this patient may have arisen in a preexisting sarcoid nodule and, therefore, represents a scar cancer. An alternative explanation for the coexistence of these two disease entities is that the patient's initial lesion was a well-defined adenocarcinoma which had subsequently become engulfed by the sarcoidosis and had metastasized.

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Dystonia musculorum deformans in pregnancy

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Dystonia musculorum deformans (DMD) is a rare neurologic disorder characterized by involuntary twisting movements and postures. To our knowledge, there have been no reported cases of a successful pregnancy in patients with this disease.

Case Report

A 23-year-old black woman, gravida 1 para 0, was referred to North Shore University Hospital at nine weeks of gestation for prenatal care.

The patient first noted an involuntary posturing of her left foot at eight years of age. During the following nine years, she noted an increasing frequency of involuntary movements and muscle spasms of her lower extremities, which initially involved the distal portions and progressed proximally. During this time, evaluation of her symptoms at the Neurologic Institute of Columbia University, NY, led to a diagnosis of DMD. There was no family history of this disease or of any other neurologic disease. The disease progressed to involve her hip and anterior abdominal muscles, thereby confining the patient to a wheelchair for five years. In addition, she had mild slurring of her speech and truncal unsteadiness. The face, neck, and back muscles were spared. The patient was treated with haloperidol, 6 mg/day, and carbamazepine, 200 mg/day, which provided only partial relief of her dystonic symptoms.

Physical examination during the first antepartum visit revealed a mildly dysarthric woman with involuntary movements of the left biceps, intorsion of the hips, and inversion and intorsion of the feet secondary to flexion contractures. Voluntary knee flexion was impossible. The anterior abdominal wall was tense, and palpation of the abdominal organs was not possible. Pelvic examination revealed an adequate gynecoid pelvis. Uterine size could not be evaluated due to a tense abdominal wall. The remainder of the physical examination was unremarkable.

An obstetrical ultrasound examination revealed an intrauterine pregnancy consistent with the patient's menstrual history. Laboratory data were remarkable for a hemoglobin count of 10.9 g/dL and a reticulocyte count of 0.5%, which was believed to be caused by the suppressive effects of carbamazepine on the bone marrow. Genetic and obstetrical counseling were provided, and the patient elected to continue with the pregnancy.

Her antepartum course was unremarkable until the 26th week of gestation, when she noted frequent episodes of dyspnea, which were associated with spasms of the abdominal wall. Arterial blood gas analyses were unremarkable. Pulmonary function tests revealed normal flow rates, with reduced volumes in total lung capacity (62% of normal), vital capacity (62%), and residual capacity (55%). These findings were consistent with her primary disease process in-

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volving the intercostal muscles. The spasms of the abdominal wall responded well to an increase in carbamazepine from 200 mg/day to 600 mg/day and a decrease in her meal volumes. The patient was discharged from the hospital on this regimen and did well until the 29th week of gestation, when she was readmitted complaining of more frequent and more intense abdominal spasms, with increasing difficulty in breathing. Arterial blood gas and pulmonary function tests were repeated, and the new results were similar to those of the previous admission. The interval of her carbamazepine administration was changed from three times a day to every eight hours. The haloperidol dosage was increased to 3 mg every eight hours with doses of 1.5 mg administered as needed. The patient responded well to this regimen.

She was readmitted at 36 weeks of gestation due to incapacitating abdominal spasms. Despite manipulation of her carbamazepine and haloperidol regimens, relief was only obtained with administration of a narcotic. At 38 weeks of gestation an amniocentesis was performed, and amniotic fluid analysis revealed a lecithin/sphingomyelin ratio of 2.5 and a phosphatidylglycerol/sphingomyelin ratio of 0.6. Oxytocin induction of labor was initiated. Uterine contractions were monitored by an internal uterine pressure transducer, which revealed a resting pressure of 10 mm Hg. The patient progressed from a cervical dilation of 3 cm to full dilation within five hours and ten minutes after oxytocin was started. After 30 minutes of second stage labor, the patient vaginally delivered a 2,940 g female infant, with Apgars of 9 and 10.

Postpartum, the patient noted an improvement in appetite, ease of breathing, and disappearance of discomfort due to abdominal spasms. Pulmonary function tests were repeated, and the results were unchanged from those obtained at 26 and 31 weeks of gestation. Her medications were readjusted to the prepregnancy regimen, and the patient was discharged from the hospital. At six weeks after delivery, the patient and her baby were doing well.

Discussion

Dystonia musculorum deformans is a rare disorder, with a known incidence of 0.299/100,000 persons in the United States.[1] It is a genetically determined disease, inherited as an autosomal dominant or recessive trait. The latter is seen in patients of Jewish descent and is associated with above average intelligence.[1] In these patients, the disease first manifests itself in early childhood, initially involving the distal limb muscles and progressing rapidly thereafter. The dominant form of the disease, which is not restricted to any ethnic group, usually appears in late childhood or adolescence and runs a more benign course.[2] Occasionally, the disease can arise de novo via gamete cell mutation.[3] Due to the rarity of DMD in the black population,[1,4] the predominant mode of transmission of this disease in this group is unknown.

Clinically, the dystonic movements may be generalized, segmental, or focal. These movements are generally not present during sleep. However, when the patient is awake, the movements can be either continuous or intermittent. The dystonic features can be voluntary or triggered by anxiety and stress. The spasmodic features have similar characteristics. However, when a sustained spasm exists, a fixed posture may result. Over a prolonged period of time, this produces soft tissue fibrosis and joint degeneration that results in contractures.[3,5]

The disease may manifest itself in a subtle manner or present abruptly. If the manifestations occur before age 15, there is a predilection for involvement of the lower extremities, with rapid and severe progression of the disease. The onset of focal dystonias, such as torticollis and blepharospasm, usually occur during middle to late life, and the course of the disease tends to be mild.[2,3]

The age of onset ranges from 2 to 42 years, with more than 93% of cases occurring by age 21.[1,3] Most patients live a normal life span; rarely does death result from the disease itself. Deaths secondary to sustained muscle spasms have been reported. Asphyxia has resulted in death when the disease involved the respiratory muscles.[6] Starvation and dehydration secondary to unrelenting spasms of the abdominal muscles have resulted in the deaths of two patients.[3,7]

The etiology of DMD remains unknown. The basis of the disease is believed to originate in the brain; however, gross and histologic analyses of the brains of affected individuals do not show any significant differences over age-matched control subjects.[3,8,9]

Present-day treatment centers on two modes of therapy: medication or surgery. Numerous drugs have been tried singly and in combination. Although results have not been uniformly successful or prolonged, medication does promote relaxation and may thereby reduce anxiety-induced dystonic movements or spasms.[1] While neurosurgery has provided variable results, even patients treated successfully have experienced relapses.[1,3] Orthopedic aids such as braces, casts, and splints are contraindicated, since they often aggravate the dystonic muscle tone.[3]

With respect to the pregnancy, there was little information that could be provided to the patient. The disease was believed to have arisen de novo, since there was no family history of DMD. The risk of inheritance in this case could not be calculated, since the mode of inheritance was unknown. Presently, there are no diagnostic tests to detect DMD in a fetus. Due to the variable penetrance of this gene, an affected child may be symptom-free for many years.

Another aspect of prenatal care is the potential teratogenic effects of haloperidol and carbamazepine. The information available is inconclusive and is summarized elsewhere.[10]

Antepartum, the patient did not experience any more symptoms until the uterus enlarged enough to displace the abdominal contents more cephalad. The initial complaints were dyspnea and decreasing appetite. This was a cause of concern, since deaths from starvation or asphyxia resulting from dystonic muscle spasms have been reported.[3,6,7] Arterial blood gas studies were unremarkable. The results of the pulmonary function tests, which showed a restrictive pattern that did not vary with the presence or absence of abdominal spasms, were attributed to disease involvement of the intercostal muscles. Subjective relief of the patient's dyspnea was obtained by increasing her medication. Her decreasing appetite was attributed to a smaller stomach capacity. Her nutritional needs were met by consuming smaller meals more frequently. The abdominal muscle spasms became painful only in the latter half of the third trimester. Readjustment of the carbamazepine-haloperidol regimen did not provide relief during that time. This is not unusual, since the relief of dystonic symptoms is not always dose related.[11] The addition of narcotic analgesics was necessary and was required more frequently as the patient approached term.

Analysis of the amniotic fluid at 38 weeks of gestation showed that this disease and the medications used to treat this patient did not appear to delay the pulmonary maturation processes in the fetus.

Increased intra-abdominal pressures secondary to muscle spasms and their possible effects on the pregnancy were of concern. However, the intrauterine pressures were measured during the delivery, and the resting pressure was noted to be 10 mm Hg, which is normal for an uncomplicated pregnancy.[12]

Improvement in symptoms was noted in the immediate postpartum period. Results of pulmonary function tests performed at two days and at seven weeks postpartum were similar to the antepartum results. Therefore, although there was evidence of DMD involvement of the intercostal muscles, the subjective dyspnea was related to the enlarging uterus.

There have been few known instances of pregnancy among patients with DMD, and none have been reported in the literature. Obviously, experience is limited and one cannot generalize on obstetrical management in these cases. Yet it can be concluded from this one case that a pregnancy can be maintained in patients with DMD and can have a successful outcome. Attentive obstetrical care with supportive maternal management must be provided. When maternal compromise is evident, timely intervention may be necessary to produce a viable fetus.

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Bilateral adrenal hemorrhage following surgery

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Bilateral adrenal hemorrhage with consequent adrenal insufficiency is a rare complication of a variety of stressful conditions, including sepsis, severe burns, cardiovascular catastrophes,[1] and extensive surgery.[2-5] Anticoagulant therapy is a contributory factor in a significant proportion of cases.[1] This complication is a life-threatening entity when the diagnosis is missed or delayed, as frequently occurs because of the subtle or misleading signs and symptoms, but it can be treated successfully when the diagnosis is promptly made. We describe a patient in whom bilateral adrenal hemorrhage with adrenal insufficiency developed after abdominal surgery. A definitive diagnosis was made by computed tomographic scanning of the abdomen, permitting initiation of specific and successful corticosteroid therapy.

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Case Report

An 81-year-old woman was admitted to the hospital for elective repair of an aorto-iliac aneurysm. The aneurysm was infrarenal, approximately six cm in diameter, and extended from 1½ cm below the renal arteries into both common iliac arteries. The patient underwent an aorto-iliac aneurysmectomy, with aorta-to-right-common-iliac and aorta-to-left-common-femoral bypass grafts, using woven Dacron. Prior to the anastomoses, 5,000 U of heparin was given intravenously; after completion of the anastomoses heparinized saline solution was infused briefly through both vessels. The evening after surgery, the patient's partial thromboplastin time (PTT) was slightly elevated (40 sec; control, 31 sec); the PTT was within normal limits the following day. Estimated blood loss during the procedure was 2,000 mL, and the patient received a transfusion with 3 units of packed red blood cells. Her vital signs remained stable throughout the procedure.

She did well until the third day after surgery, when the blood hemoglobin concentration dropped to 8.5 g/dL, from 10.9 g/dL on the first day after surgery. Her temperature spiked to 102°F, and the leukocyte count rose to 18,300/mm^3, with 83% polymorphonuclear leukocytes, 11% band forms, 3% lymphocytes, and 3% monocytes. Blood cultures were drawn, and the patient received a transfusion with 2 units of packed red blood cells, resulting in a rise of the hemoglobin level to 11.6 g/dL. On the sixth day after surgery, nausea and vomiting developed, and the patient complained of pain over the right scapula. Her blood pressure and serum electrolyte levels were normal, and an electrocardiogram showed no acute changes. The nausea and vomiting persisted, and the back pain migrated to the right flank. She became drowsy and depressed. During the next two days, severe abdominal pain and tenderness to palpation developed, and she became increasingly lethargic. On the ninth day after surgery her temperature was 101°F and the leukocytosis persisted. Multiple blood and urine cultures were negative.

A computed tomographic (CT) scan of the abdomen, done on the ninth day after surgery, disclosed no evidence of subdiaphragmatic or intra-abdominal abscess. A gallium scan demonstrated mildly increased uptake along the graft, but no abnormalities to suggest wound infection or abscess. The lethargy, fever, vomiting, and abdominal pain persisted. Despite the negative blood cultures, the patient was treated empirically with cefoxitin, tobramycin, and oxacillin. She gradually became semicomatose, responding only to painful stimuli.

On the ninth day after surgery, her serum sodium concentration was 133 meq/L, and

FIGURE 1. Abdominal CT scan on the 11th day after surgery, showing marked enlargement of both adrenals (arrows), consistent with bilateral adrenal hemorrhage.

the potassium concentration was 3.2 meq/L. The next day, the sodium level decreased to 129 meq/L, and the potassium level rose to 4.7 meq/L. On the 11th day after surgery the sodium level was 122 meq/L, and the potassium level was 5.2 meq/L. Her blood pressure was 134/60 mm Hg.

The abdominal CT scan was repeated on the 11th day and demonstrated bilateral enlargement of the adrenals, consistent with adrenal hemorrhage (Fig 1). A review of the earlier CT scan showed that similar findings had been present then too (Fig 2). A blood sample that had been drawn earlier on the 11th day was sent for cortisol determination, and the patient was given intravenous hydrocortisone hemisuccinate sodium, 50 mg every six hours. Two hours after the second dose, she was awake and alert, with a temperature of 99.3°F and a blood pressure of 130/70 mm Hg. Plasma cortisol concentration in the pretreatment blood sample was later reported as less than 2 μg/dL. Her condition continued to improve, and she was placed on a regimen of oral cortisone acetate, 37.5 mg daily, and fludrocortisone, 0.1 mg daily. On the 24th day after surgery, 13 days after the start of corticosteroid therapy, an intravenous cosyntropin test was done 12 hours after a dose of cortisone acetate; there was no significant rise in serum cortisol. Later that day, she was discharged from the hospital, feeling well and alert.

Discussion

The diagnosis of adrenal hemorrhage with adrenal insufficiency is especially likely to be missed or delayed when the disorder occurs as a postoperative complication; the signs and symptoms may be mistakenly attributed to more common complications such as intra-abdominal infection and sepsis. This was the case in the patient described in this report. Her increasing abdominal discomfort, lethargy, fever, and leukocytosis were initially ascribed to intra-abdominal infection, and antibiotic therapy was administered. It was only during a computed tomographic examination of the abdomen, in search of a possible abscess, that the diagnosis of bilateral adrenal hemorrhage was made. Though corticosteroid therapy was not started until the 11th day after surgery, the characteristic abnormalities were present on the CT scan taken two days earlier and might also have been present on scans taken still earlier, had the diagnosis been considered when the symptoms of abdominal pain, fever, and leukocytosis first appeared.

Seven cases have been previously reported in which the diagnosis of bilateral adrenal hemorrhage was made by CT scan of the abdomen[5-9]; in four of these cases[6,8,9] anticoagulant therapy had been given. In nearly all the cases, the diagnosis was made relatively late. With a high index of suspicion, it should be possible to make a much more prompt diagnosis, indeed as soon as the condition develops. This complication should be suspected in any severely stressed patient whose condition suddenly deteriorates, and who has symptoms of abdominal pain, fever, and lethargy, even before hypotension and the characteristic electrolyte abnormalities of adrenal insufficiency appear. Increased suspicion is appropriate in elderly patients or among patients who are receiving anticoagulants or have a tendency to bleed.

When adrenal insufficiency is suspected, the usual clinical reflex is to measure the plasma cortisol concentration, but the finding of a normal plasma cortisol level does not rule out adrenal insufficiency. Under conditions of severe stress, the patient may have low normal or even normal levels of plasma cortisol.[10] An unequivocal diagnosis of adrenal insufficiency can still be made in such cases, based on the absence of an increase in cortisol concentration after stimulation by adrenocorticotropic hormone.

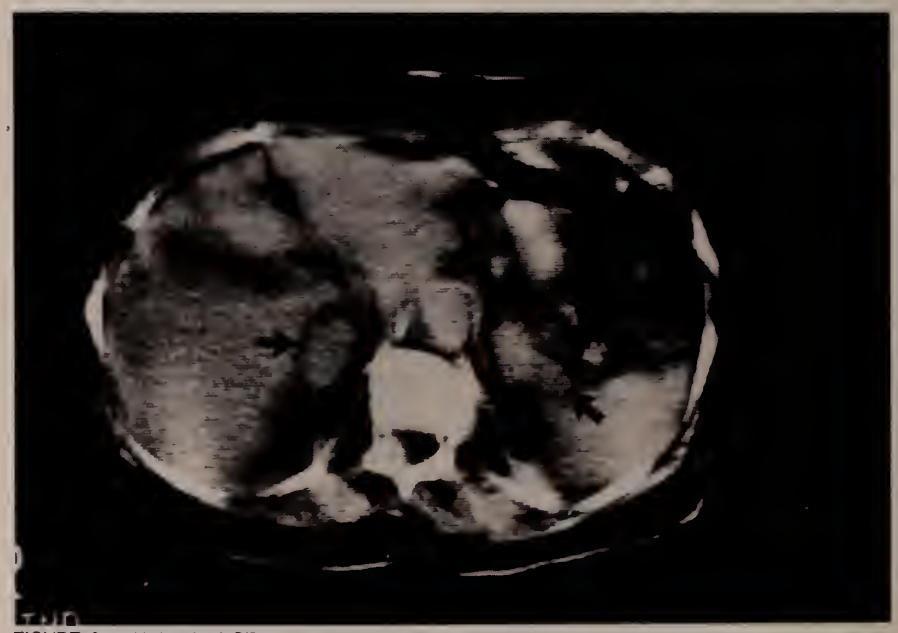

FIGURE 2. Abdominal CT scan on the ninth post-operative day. The findings are essentially the same as in the later CT scan.

FIGURE 3. Abdominal CT scan 16 months after surgery. **Left,** maximum diameter of the right adrenal gland; **Right,** maximum diameter of the left gland; both are within the normal range.

In any case, waiting for a report of cortisol levels in cases of suspected adrenal hemorrhage with adrenal insufficiency introduces a dangerous, potentially fatal delay, whereas CT scanning offers the possibility of real-time diagnosis. It would seem desirable, therefore, to apply this powerful diagnostic technique as early as possible when adrenal hemorrhage is suspected, so that the patient can be treated for adrenal insufficiency, and the diagnosis can be confirmed later by endocrine testing.

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Endobronchial osseous foreign body: Computed tomographic evaluation

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The diagnosis of an aspirated foreign body is not difficult if there is a suggestive history or if a chest radiograph demonstrates a foreign object or signs of bronchial occlusion (air trapping, atelectasis, or mediastinal shift). When the history and radiographic findings are not helpful, accurate diagnosis is more difficult. Furthermore, bronchoscopic examination may not reveal the foreign body, even in suspected cases.[1] We describe the utility of computed tomographic (CT) scanning in the diagnosis and localization of an occult endobronchial foreign body.

Case Report

A 58-year-old man was admitted to the hospital for treatment of fever, night sweats, and cough productive of purulent sputum of four weeks' duration. He admitted to heavy cigarette smoking and alcohol use for many years, but denied any episode of aspiration.

On examination, bronchial breath sounds and crackles were heard over the upper left chest. A chest radiograph revealed consolidation and cavitation in the upper lobe of the left lung (Fig 1). Sputum specimens for routine culture, cytologic examination, and staining for acid-fast bacilli were unrevealing. Fiberoptic bronchoscopic examination disclosed a hard, fixed, polypoid mass extending from the left lower lobe bronchus and occluding the left upper lobe bronchus. Biopsies of the lesion revealed necrotic, trabeculated bone and calcific debris. A CT scan of the chest showed an irregularly shaped calcific mass at the bifurcation of the left main bronchus (Fig 2). The bronchi were patent distal to the mass. Consolidation with multiple cavities was confirmed in the apical-posterior segment of the left upper lobe. The CT examination was otherwise unremarkable.

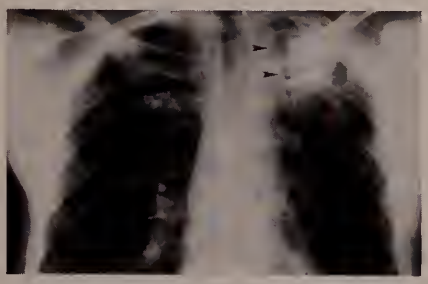

FIGURE 1. Posteroanterior chest radiograph showing large irregular opacity with several cavities (arrowheads) in the apex of the left upper lobe. No endobronchial mass was noted, and the lungs were otherwise clear.

Rigid bronchoscopy was performed, and a 1.0 × 1.0 × 1.2 cm bony mass was removed from the distal left main and proximal left lower lobe bronchi. Although the mass fragmented during removal, it appeared on gross examination to represent a vertebra from a chicken (Fig 3). The patient's fever subsided, and his condition improved rapidly on intravenous ampicillin therapy. He was discharged from the hospital on oral penicillin therapy after 14 days.

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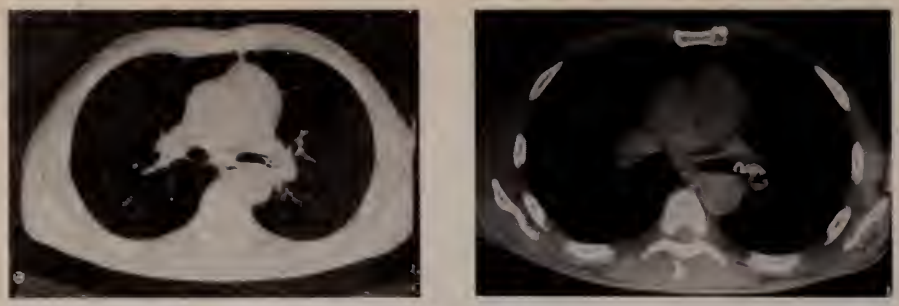

FIGURE 2. CT images of the chest at the level of the bifurcation of the left main bronchus. **Left,** 4-mm-thick section shows spiculated endobronchial calcific opacity containing a lucent center, suggesting the spinal canal of a vertebra. **Right,** 2-mm-thick section, slightly inferior to the section seen at left. Bone density window emphasizes cortical density and central lucency of the osseous foreign body. The bronchus (arrow) to the superior segment of the left lower lobe is patent, with its origin positioned a few millimeters beyond the carina between the upper and lower lobe bronchi. The bronchus to the upper lobe (not shown because of respiratory motion artifact) was patent.

Discussion

In this patient, fiberoptic bronchoscopy preceding CT examination showed a firm endobronchial mass, possibly a foreign body. After histologic examination revealed necrotic bone, CT scanning was employed not only to confirm that impression, but also to map the extent of endobronchial obstruction and adjacent parenchymal disease.

When a foreign body causes adjacent bronchial mucosa to become inflamed or edematous, the extent and even the presence of the foreign body may be difficult to assess by bronchoscopy alone.[1]

FIGURE 3. Four osseous fragments were removed with the rigid bronchoscope. The largest piece resembles a vertebra.

The demonstration by CT scanning of localized endobronchial bone led to the appropriate choice of rigid bronchoscopy rather than thoracotomy for the removal of the foreign body. If removal of the aspirated bone by rigid bronchoscopy had proved unsuccessful and surgical resection had been necessary, then a description of the foreign body and associated lung disease from the CT scan would also have proved helpful to the thoracic surgeon.

Imaging methods to detect occult or radiolucent foreign bodies include fluoroscopy, xeroradiography, and computed tomography.[2-4] In vivo studies have shown CT scanning to be superior to plain radiography in demonstrating endobronchial foreign bodies.[5,6] Because CT scanning can resolve minor differences of physical density with great sensitivity, it is useful in detecting slightly radiopaque foreign bodies (such as glass, aluminum, and some plastics) as well as material with a density similar to that of human soft tissues (animal cartilage, some plastics, thorns, and wood in situ for more than 48 hours).[7] However, a CT scan of the chest can fail to detect small intrathoracic lesions unless meticulous attention is paid to the examination technique. Continuous or overlapping sections through suspicious regions, finely collimated for optimal detail, are usually necessary for an adequate study.[8]

Given the exposure to radiation, the cost, and the manpower involved in CT scanning, we do not recommend this imaging technique as a primary means of assessing aspirated foreign bodies. However, as in this patient, a role for CT scanning is suggested when an occult foreign body is suspected and it is important to determine the extent of associated disease. A CT scan may also help to identify small, distal foreign bodies, or material hidden from the bronchoscopist's view by secretions, edematous mucosa, or granulation tissue. When a patient is suspected of having aspirated multiple radiolucent foreign bodies which may have been missed on bronchoscopic examination, CT scanning should be considered.

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Address correspondence to Editor, New York State Journal of Medicine, *420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication. All letters are personally acknowledged by the Editor.*

Use of carbidopa as an adjuvant to levodopa/carbidopa therapy in patients with Parkinson's disease

TO THE EDITOR: Levodopa treatment for patients with Parkinson's disease has been facilitated by the introduction of extracerebral dopa decarboxylase inhibitors. Extracerebral dopa decarboxylase is an enzyme found throughout the body and in concentrated amounts in the gut, liver, and around capillaries. It controls the conversion of levodopa to dopamine. Carbidopa blocks the action of extracerebral dopa decarboxylase in the gut and liver predominantly, thus blocking the conversion of levodopa to dopamine in the gut and yielding increased plasma levodopa levels.

Patients require at least 75 mg/day of carbidopa (Lodosyn™) to fully inhibit extracerebral dopa decarboxylase, regardless of body weight.[1] It is estimated that carbidopa doubles the bioavailability of oral levodopa.[2] The increased bioavailability of levodopa results in a higher intracerebral levodopa concentration and better control of Parkinson's disease.

Concomitant with the higher plasma levodopa levels are lower plasma dopamine levels. This is beneficial, because it is dopamine that causes the nausea and vomiting that may be associated with levodopa treatment. The coadministration of an extracerebral dopa decarboxylase inhibitor with levodopa decreases the nausea and vomiting.[3-8]

Because the extracerebral dopa decarboxylase inhibitors do not themselves cross the blood-brain barrier, they cannot inhibit the intracerebral conversion of levodopa to dopamine, which is a prerequisite for levodopa's antiparkinson effect.

There are two groups of patients who have particular difficulty using levodopa/carbidopa, even at low doses. These patients usually receive less than 75 mg/day of carbidopa. One group of patients with Parkinson's disease and dementia are unable to tolerate low doses of levodopa/carbidopa because of adverse effects probably related to an increased sensitivity to the effects of intracerebral dopamine. These effects include dyskinesia and increased mental symptoms. A second group of patients without dementia are unable to tolerate low doses of levodopa/carbidopa because of adverse effects related to a relative excess of extracerebral dopamine. These effects include nausea and vomiting.

Case Report. Seven patients with Parkinson's disease and mild dementia[9] were unable to tolerate at least 75 mg/day of carbidopa in levodopa/carbidopa. The mean age of these seven patients was 75.3 years (range, 52–83 years). The mean duration of the Parkinson's disease was 5.0 years (range, 3–11 years). All of the patients had been treated previously with anticholinergic drugs or amantadine (Symmetrel™), but these drugs had been discontinued because of increased changes in mental status. Two of these patients had been treated with bromocriptine (Parlodel™), a dopamine agonist, but this treatment had also been discontinued because of changes in mental status.

The mean duration of treatment with levodopa/carbidopa was 3.9 years (range, 2–6 years). Attempts to increase the dosage of levodopa or levodopa/carbidopa resulted in worsening of the patients' Parkinson's disease symptoms. The availability of carbidopa alone (Lodosyn™) led to a new strategy. The patients received carbidopa, 25 mg/day increased each week, in addition to their dose of levodopa/carbidopa, until the Parkinson's disease improved or the patients experienced adverse effects.

The patients were evaluated every two weeks using a modification of the New York University Disability Scale.[10] They were evaluated by a physician who was unaware of the medication the patients were receiving. A score of 0 indicated no disability and a score of 100 indicated complete disability. The study was continued for one year.

The second group of patients consisted of three patients with Parkinson's disease who did not have dementia and who had been unable to tolerate levodopa/carbidopa due to nausea and vomiting. The mean age of the three patients was 72.3 years (range, 71–74 years). The mean duration of the Parkinson's disease was 3.7 years (range, 1–8 years). All three patients had been treated with anticholinergic drugs or amantadine, but this treatment had been discontinued because of no effect (two patients) or adverse effects (one patient). None of the patients had been treated with bromocriptine.

Carbidopa therapy was begun at a level of 25 mg/day in two divided doses, and was increased by 25 mg/day each week until a daily dose of 75–100 mg/day was achieved. At this time, levodopa, 50 mg/day, was added to the first daily dose of carbidopa. The dose of levodopa was then increased by 50 mg/day until a therapeutic response was achieved or adverse effects occurred.

Among the seven patients with Parkinson's disease and dementia, three patients showed noticeable improvement (they improved by at least 50% on the NYU Disability Scale). However, for the group as a whole, the mean score decreased by 5%, from 43.6 (standard error of the mean (SEM), ±3.3) to 41.4 (SEM, ±5.0) and was not significant. The four patients who did not improve were eliminated from the trial because of adverse effects including increased changes in mental status (three patients) and syncope (one patient). While the number of patients is too small to draw any conclusions, it is apparent that among some patients with dementia, adding carbidopa to their regimen of levodopa/carbidopa is useful.

All of the three patients in the second group improved by at least 50%, and none experienced nausea and vomiting. The mean score (NYU Disability Scale) decreased by 64%, from 39 (SEM, ±4.5) to 14 (SEM, ±2.0) (44%), and this was significant ($p \leq 0.05$). An improvement was noted in two of the patients with as little as 200 mg of levodopa and 75–100 mg of carbidopa. This improvement is not surprising, as it would be expected that if these patients could be made to tolerate levodopa, their Parkinson's disease symptoms would improve.

Discussion. Carbidopa alone is a valuable adjuvant in the management of patients with Parkinson's disease. Approximately 30% of patients with Parkinson's disease also suffer from dementia. Among patients with Parkinson's disease and dementia who experience increasing Parkinson's symptoms, attempts to alleviate these symptoms by administering levodopa or levodopa/carbidopa often result in increasing changes in mental status without improving the Parkinson's disease.[11] However, by adding carbidopa to these patients' levodopa/carbidopa regimen, we were able to improve the Parkinson's symptoms in three patients (without in-

creasing their mental disorder). Improvement was achieved because the additional carbidopa completely blocked extracerebral dopa decarboxylase and allowed a higher percentage of the administered levodopa to reach the brain—enough to improve the Parkinson's disease, but not enough to worsen the dementia.

In patients who are unable to tolerate low doses of levodopa/carbidopa because of nausea and vomiting, carbidopa alone is also useful. The administration of carbidopa first and later addition of levodopa permitted these patients to tolerate levodopa—something they could not do when both drugs were administered simultaneously.

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Subclinical pituitary apoplexy

TO THE EDITOR: Spontaneous hemorrhagic necrosis in a pituitary adenoma (pituitary apoplexy) is usually a catastrophic event with a high likelihood of fatality if not promptly recognized and treated.[1-5] The common clinical features are sudden onset of severe headache, visual disturbances, nausea and vomiting, changes in the level of consciousness, nuchal rigidity, and fever. The syndrome usually evolves over a 24- to 48-hour period, with progressive deterioration of the patient's clinical status. I describe a patient with recurrent syncopal episodes—an unusual finding—as the clinical evidence for pituitary apoplexy.

Case Report. A 67-year-old woman was admitted to the hospital in December 1982 for treatment of episodes of fainting with loss of consciousness for periods of one to five minutes. She had had hypertension for the past 20 years, for which she was taking timolol, 10 mg twice a day. She denied having headaches but confirmed symptoms of blurred vision, nausea, and vomiting before fainting. She denied coughing or sneezing prior to the onset of fainting, and she had experienced no recent head trauma.

On physical examination the patient was conscious but lethargic. Her temperature was 39°C. Except for mild ptosis of the right eye, there were no neurological deficits. Funduscopic evaluation was unsatisfactory because of bilateral cataracts. Her blood pressure in the supine position was 145/70 mm Hg and on standing was 65/45 mm Hg. The pulse rate in the supine position was 84/min and regular. The heart sounds were normal, with no murmurs. On examination the respiratory system and abdomen were within normal limits. Initial screening laboratory tests were normal, except for a potassium level of 3.0 mEq/dL.

The patient was treated with intravenous normal saline and potassium supplements, and the timolol was discontinued.

Cardiac evaluation showed no evidence of damage or arrhythmia to account for the syncopal episodes. Examination of visual fields showed bitemporal hemianopia. A skull radiograph showed erosion of the anterior clinoid process and evidence of an enlarged sella turcica. A computed axial tomographic (CAT) scan of the brain (Fig 1) confirmed a sellar mass with suprasellar extension.

The patient was given cortisone acetate and L-thyroxine supplements after blood was drawn for cortisol levels and thyroid function tests. Her condition improved dramatically with this regimen. The results of endocrine evaluation were as follows: cortisol, 1.4 μg/dL (am) (normal range, 8-27 μg/dL); cortisol, 1.1 μg/dL (pm) (normal range, 3-16 μg/dL); prolactin, 13.3 ng/mL (normal range, 0-25 ng/mL); T_4, 3.0 μg/dL (normal range, 4-14 μg/dL); T_3 resin uptake, 26% (normal range, 24-36%); thyroid stimulating hormone, 1.7 μIU/mL (normal range, 1-8 μIU/mL). Growth hormone levels after insulin-induced hypoglycemia are shown in Table I.

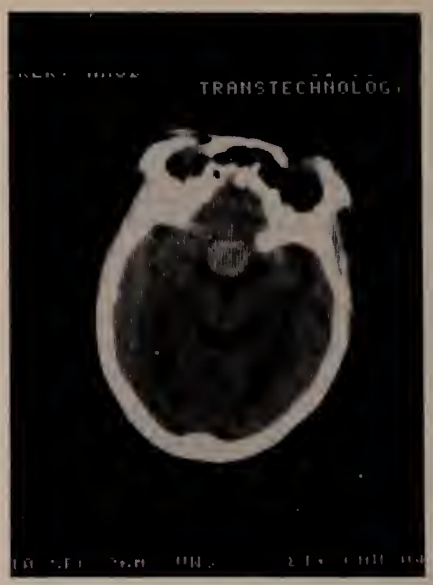

FIGURE 1. CAT scan of the brain showing sellar mass.

The patient was transferred to a neurologic institute, where she underwent transsphenoidal removal of the pituitary tumor three weeks after the onset of syncopal episodes. Analysis of the tumor showed evidence of hemorrhagic necrosis in a nonfunctioning pituitary adenoma. The patient's recovery was uneventful, and visual acuity returned to normal.

Discussion. Hemorrhagic necrosis in pituitary tumors is usually manifested by a preponderance of neurologic features secondary to acute expansion of the tumor, rather than to features of acute panhypopituitarism.[3] This finding prompted Conomy and associates[3] to propose the term "acute tumorogenic parasellar compressive syndrome" to describe hemorrhagic necrosis in a preexisting pituitary tumor, and the term "pituitary apoplexy" to describe infarction or hemorrhagic necrosis in a nontumorous pituitary gland. The pathogenesis of this patient's syncopal episode was a result of acute pituitary adrenal insufficiency. The marked improve-

TABLE I. Growth Hormone Levels After Insulin-Induced Hypoglycemia

Time (min)	Human Growth Hormone (ng/mL)*	Plasma Glucose Level (mg/dL)
0	<1	120
10	<1	100
20	<1	81
30	<1	48
45	1	43
60	1	38

* Normal basal level of human growth hormone, 0-5 ng/mL.

ment noted with cortisone acetate therapy supports this hypothesis.

The patient had none of the usual predisposing causes of hemorrhagic necrosis: coughing, sneezing, pituitary irradiation, estrogen therapy, anticoagulation therapy, bromocriptine therapy, and diabetic ketoacidosis.[5] Rovit and Fein[6] have suggested that spontaneous hemorrhagic necrosis in a pituitary tumor is due to impaction of the pituitary blood supply at the notch of the diaphragma sellae, rendering the tumor ischemic. Pituitary apoplexy was not considered prior to surgery because of the absence of severe headaches. However, the sudden onset of syncopal episodes and lethargy suggested an acute event in a preexisting pituitary tumor. The fact that the patient's visual fields returned to normal after surgery further attests to the sudden increase in the size of the tumor. The absence of any headaches under such circumstances is highly unusual, prompting the use of the term subclinical apoplexy.

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Intramuscular pleomorphic lipoma

TO THE EDITOR: Tumors of adipose tissue occasionally display atypical histologic foci, which are sometimes interpreted as malignant. Several authors[1-4] have described a series of lipomatous neoplasms with a distinctive histologic appearance, which they have designated pleomorphic lipoma. This tumor occurs in the subcutis—generally of the head and neck—and has a benign clinical course, with surgical removal usually being curative. Evans et al[5] and Kindblom et al[6,7] described tumors with a similar, if not identical, histologic picture which were intramuscular and had a tendency to recur in a significant percentage of cases following surgery; the authors called these lesions atypical lipomas[5] or atypical intramuscular lipomas.[6,7] None of the reported tumors metastasized after long follow-up periods. The classification of these intramuscular tumors is further complicated by the fact that some authors consider them to be well-differentiated liposarcomas.[2]

We present a case of an intramuscular pleomorphic (atypical) lipomatous neoplasm and discuss the classification of this lesion and its clinical implications.

Case Report. A 27-year-old man had noted a growing, painless mass in his left anterior thigh during the year prior to admission. The patient denied any limitation of movement due to the mass. Physical examination revealed a fist-sized mass in the anteromedial aspect of the mid-third of the left thigh. The mass was soft, nontender, and without evident vascular engorgement.

Computed tomography using contrast revealed a well-delineated mass in the anterior muscular compartment of the left vastus medialis, without infiltration of the adjacent intramuscular fascia or subcutaneous tissue. The mass had a mean density similar to that of fat. The clinical impression was that of an infiltrating lipoma of the left anterior thigh. A block resection of the lesion was performed.

The surgically resected specimen consisted of a portion of vastus medialis muscle with an oblong, yellow, rubbery mass firmly adherent to the anterior surface of the muscle. The entire specimen measured 14 × 11 × 5 cm, and the tumor measured 8 × 5 × 4 cm. The tumor appeared well circumscribed on the superficial surface. The cut surface was yellow with focal myxoid areas. Along the deep surface, the tumor grossly infiltrated the muscle.

On microscopic examination, the tumor displayed several patterns. For the most part, it was composed of mature fat cells. There were foci of loose collagenous tissue arranged in sheets or as relatively thin bands insinuated between fat cells. The fibrous areas generally contained cells with dark oval to spindle shaped uniform nuclei (Fig 1). These areas sometimes merged into more cellular areas that contained cells with larger, more variable nuclei—either vesicular or hyperchromatic (Fig 2). Occasional multinucleated cells of the floret type were present (Fig 3). No lipoblasts were noted. A rare mitotic figure was identified. At its periphery, the tumor infiltrated the adjacent striated muscle.

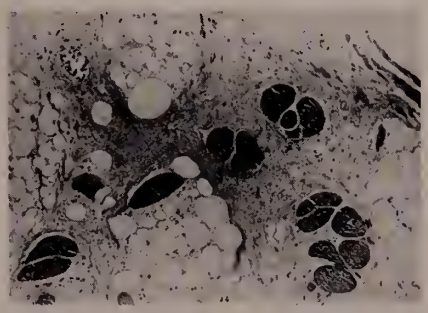

FIGURE 1. Lipoma with spindle-cell component infiltrating skeletal muscle (hematoxylin-eosin stain; original magnification × 63).

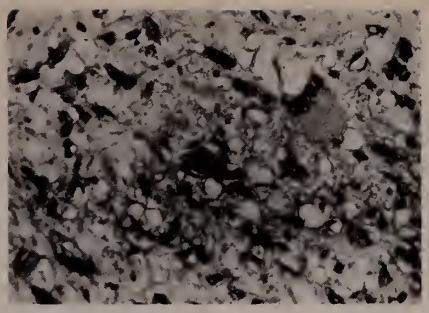

FIGURE 2. Pleomorphic lipoma with cells demonstrating variation in nuclear size and shape (hematoxylin-eosin stain; original magnification × 200).

There has been no recurrence of the lesion in more than three years of postsurgery follow-up.

Discussion. Lipomas are among the most common benign neoplasms encountered clinically. For the most part, they are subcutaneous, well circumscribed, and composed of mature adipocytes. Occasionally they display focal areas of a different morphology, leading to the designations angiolipoma, spindle-cell lipoma, or pleomorphic lipoma.[3] The recognition by Enzinger[1] that pleomorphic lipomas behaved in a benign manner was of particular importance, because the highly atypical cells and areas of fibrous and myxoid change were often diagnosed as liposarcoma, leading to unnecessary radical surgery. Subcutaneous lipomas, including their morphologic variants, rarely recur after surgery.

Intramuscular lipomas, on the other hand, are often infiltrative lesions, and recurrences are common following at-

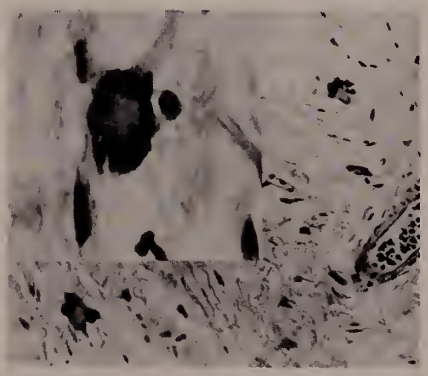

FIGURE 3. Two floret cells with peripheral nuclei (hematoxylin-eosin stain; original magnification × 100). Inset, a typical floret cell (hematoxylin-eosin stain; original magnification × 250).

tempts at surgical removal. While these lesions are usually composed of mature adipocytes, focal histologic variants identical to those in the subcutis are also occasionally observed. Angiolipoma, for example, while most often a circumscribed subcutaneous tumor, infiltrates adjacent normal tissue when it arises in striated muscle.[8] Also minor histologic differences may occur; for example, subcutaneous angiolipomas may have thrombosed vessels, a feature not seen in the intramuscular counterpart.

Features seen in subcutaneous pleomorphic lipoma—fibrosis, myxoid change, floret cells, and association with areas of spindle cell lipoma—can also occur in intramuscular lipomas; in this case, however, the terminology is not consistent. These lesions have been designated atypical lipoma, atypical intramuscular lipoma, and well-differentiated liposarcoma on the basis of their location, in spite of their histologic similarity to the subcutaneous lesion. The term angiolipoma is used to designate both the subcutaneous and intramuscular tumor.

We think that this intramuscular lesion is the histologic counterpart of the subcutaneous pleomorphic lipoma. It differs from its subcutaneous relative solely in its infiltrative behavior—a situation similar to that observed with intramuscular angiolipoma. The high rate of recurrence of these lesions is due to a lack of appreciation by surgeons of their tendency to infiltrate. In the series described by Kindblom et al,[6,7] only rarely did intramuscular lipomas recur following surgery, because of the policy at the University of Goteborg to perform a wide en-bloc excision for intramuscular lipomas, rather than mere enucleation or excision with a narrow margin of muscle. It should be emphasized that none of the intramuscular lesions in the series reported by Evans[5] and Kindblom et al[6,7] metastasized, even after multiple recurrences. We believe that a neoplasm without the capacity to metastasize should not be classified as malignant.

The clinical behavior of lipomas and their morphologic variants depends mainly, if not entirely, on their location. Subcutaneous neoplasms tend to be circumscribed and can therefore be removed with little normal margin, whereas intramuscular lipomas tend to infiltrate and should be resected with a wide margin to avoid recurrence. The different terms used to designate this morphologic variant of lipoma into separate nosologic entities are confusing and unnecessary. It is important, however, that this morphologic variation of lipoma, either in the subcutaneous or intramuscular locations, not be diagnosed as liposarcoma, leading to unnecessarily radical surgery.

We suggest that this lesion be designated as intramuscular pleomorphic lipoma; intramuscular, to call attention to its propensity for infiltrative growth with the resulting implication for wider surgical excision, and pleomorphic, because of its histologic similarity to the well-characterized subcutaneous tumor.

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GERIATRIC MEDICINE ANNUAL 1986

Edited by Richard J. Ham, MD. 276 pp, illustrated. Oradell, NJ, Medical Economics Books, 1986, $32.95 (hardcover)

This book is a collection of articles dealing with common health care issues of older adults. In his introduction, Richard Ham, MD, states that the purpose of this book, as well as future Annuals, is to serve as an overview of information on important health care topics. For the reader who desires more in-depth information, references are cited in each chapter. The editor welcomes the readers' suggestions for possible subjects of future publications.

The editor and many of the contributors are respected authors in geriatric medicine. Dr Ham is well known in family practice circles—as well as gerontologic organizations—as an innovative teacher and author. The names of other contributors to this publication such as William Applegate, MD, Paul Gilber, MD, Peter J. Lamy, PhD, and Rein Tideiksaar, PhD, are also well known to this reviewer. The reader should be assured that the editor made every attempt to secure the contributions of many of the best known authorities in geriatric medicine.

Because this is a review of geriatric medicine topics, the contents address issues in many medical specialties and disciplines. Medical specialties such as psychiatry, surgery, gynecology, endocrinology, cardiology, and urology are all represented. Other important areas such as sexual problems, ethical issues, and pharmacology are also appropriately included in this reference. Because this is an ongoing series, the editor did not intend for this to be an exhaustive text but rather one that could be used by the health care practitioner as a review of certain areas. The reader should not confuse this publication with a "clinics" format because there are multiple areas addressed within the volume.

This reviewer felt that in general the clarity and style of each chapter was excellent. As with any other publication, there was some variation in the amount of detail covered in each chapter. An example of this unevenness was the chapter on the use of new antidepressants excellently presented by Dr Moore; the chapter included a detailed discussion of the classification of drugs, the role of illness and depression, diagnostic work-up of the depressed patient, and the pharmacology of antidepressant medication. In comparison, the chapter on the use of estrogen was too superficial and glossed over important areas such as osteoporosis and screening for the woman at high risk for cancer. This inconsistency, however, was not enough to detract from the overall quality of the book.

This book compares favorably to the other annuals published. The value to the practitioner interested in geriatric medicine is that books of this type act as concise reviews and that the reader does not have to perform a literature search of the topic. Because publications like *Geriatric Medicine Annual* are updated periodically, the practitioner may be assured of current information when he or she invests in a book series.

This book is recommended for the clinician who cares for older adults. Although other publications are similar, Dr Ham's book did cover topics necessary for the care of the elderly patient. Hopefully this will be the first of an ongoing series.

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PRACTICAL GERIATRIC THERAPEUTICS

By Richard W. Sloan, MD. 335 pp, illustrated. Oradell, NJ, Medical Economics Books, 1986. $24.95 (paperback)

This book provides a readable review of clinical pharmacology and important aspects of drug metabolism and response in geriatric patients. The author is a Clinical Assistant Professor in the Department of Family and Community Medicine at the Milton S. Hershey Medical Center of the Pennsylvania State University of Medicine, and Associate Director of the Family Practice Residency Program at Lancaster General Hospital, Lancaster, Pennsylvania. He holds a degree in pharmacology and teaches clinical pharmacology to family practice residents.

The first chapter covers relevant demographic data regarding the aging population and contains a brief summary of the physiological changes of aging. This chapter is a bit of a digression from the subject at hand. The author provides preventive health guidelines that could possibly increase life expectancy. He also makes the argument that early identification and treatment of those people at risk for chronic disease could forestall premature organ failure from diseases such as diabetes mellitus and hypertension, and therefore delay or prevent the period of disability prior to death. This would lead to a healthier elderly population requiring less medical care. However, at present we are faced with a growing elderly population, many of whom are still afflicted with one or more chronic diseases and treated with one or more medications; this is the issue Sloan addresses in the remainder of the book.

The second chapter provides more facts regarding the extent of drug use in the elderly and the problem of iatrogenesis in this population. The results of several studies are cited, including those concerned with drugs implicated in adverse drug reactions. The problem of patient compliance is discussed and practical guidelines are given for prescribing drugs for the elderly, keeping in mind the old admonition of "first, do no harm." Many of these guidelines involve the formulation of a "therapeutic plan," a concept fully developed in Chapter 4. It is used as a framework for discussing the various drug categories in the second section of the book. The development of a therapeutic plan involves identifying etiologic factors for the condition being treated, considering non-drug treatment, choosing an initial drug (which involves evaluating drug efficacy and potential side effects in the patient being treated, and choosing a drug accordingly), determining the initial dose, titrating the dose, adding a second drug, and monitoring drug therapy. To better understand these concepts, the author prefaces the chapter with a section on differences in pharmacokinetics (drug absorption, distribution, metabolism, and excretion) and pharmacodynamics (drug effects on the body) in the elderly patient. Two informative chapters follow on interpreting drug levels in elderly patients and the mechanisms behind drug interactions. Both of these chapters are filled with

common and not-so-common examples that enhance the discussions.

The second section of the work discusses cholinergic and anticholinergic drugs. It contains, as do most of the subsequent chapters, a review of pertinent physiology that serves as an effective springboard for the individual drug descriptions that follow. The clinical information in these chapters is comprehensive without being burdensome, and one comes away from each chapter with a sense of familiarity with the drugs being discussed that usually comes only with experience. The other drug categories covered in the following chapters are the following: sympatholytic drugs, vasodilators, diuretics, digitalis glycosides, antiarrhythmics, antiplatelet drugs, anticoagulants, acetaminophen, narcotic analgesics, nonsteroidal anti-inflammatory drugs, glucocorticoids, uricosuric agents, xanthine oxidase inhibitors and colchicine, antibiotics, theophylline, antiparkinsonian drugs, drugs used in gastrointestinal diseases, and hormones.

This book is by no means a comprehensive text of geriatric medicine or pharmacology, but for its size it contains a significant amount of useful information and recommendations. Dr Sloan's goal in writing this book was to provide a " 'core content' of clinically relevant information that will facilitate the safe and effective use of drugs in the elderly," and he succeeds in doing so. Although the book is geared towards the ambulatory patient, it is equally applicable in an acute or chronic care setting. It is a relatively up-to-date review of common drugs used in treating the elderly. The only controversial statement found that is worth commenting on is related to the drug ranitidine, which Sloan states has not been associated with confusion, disorientation, or hallucinations. This is somewhat in question at present; significant CNS symptoms should be considered possible side effects until further studies are completed on this drug.

The main strength of this book is that because of its organization and style it may comfortably be read from cover to cover. It is therefore more likely to benefit the reader than other texts considered more comprehensive but less likely to be read in their entirety. I consider the book a useful addition to the medical literature.

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GROWING OLD, STAYING YOUNG. WHAT MEDICINE AND SCIENCE ARE DOING TO MAKE AGING A NATURAL PART OF A HEALTHIER AND LONGER LIFE

By Christopher Hallowell. 309 pp. New York, William Morrow & Company, 1985. $17.95 (hardcover)

Bookstores are filled with self-help books on a wide variety of medically related topics. When this literature is written by a nonphysician the medical community often will not fully accept the validity of the work because the author is not a scientific "authority." When a book is written by a qualified medical person, the validity and value of the work are sometimes diminished because medical concepts and terminology are "translated" or simplified for lay readers. It is unfortunate that the medical community is biased in this way about potentially valuable and meaningful books for general readers.

Christopher Hallowell's *Growing Old, Staying Young* falls into the category of being an accurate and comprehensive account of current theories and aspects of aging in America, written by a lay person with no formal background in medicine. The impetus for writing this book was the author's experience with the death of his parents; his father from cerebrovascular accidents and pneumonia, and his mother from complications of Alzheimer's disease.

Hallowell's touching and accurate account of his mother's progressive decline is one that many physicians outside of the geriatric discipline should read carefully. He cites as authorities on the various topics covered well known and recognized physicians and health care professionals in the geriatric field from many institutions across the United States. He discusses interesting and important concerns of the middle-aged and older adult. Some of these are very sensitive and often unaddressed concerns that are shared by most patients. Topics covered include physiological aspects of normal aging, current theories, cellular changes, advice on nutrition, exercise, and preventive health care practices. Issues about preparing for retirement and problems of retirement communities are also discussed. Normal sexual changes and social myths are frankly addressed.

Throughout the book the author stresses preventive measures, along with the "use it or lose it" philosophy. In each chapter he cites additional sources of information written for the lay reader. He also includes a glossary of terms written for the nonphysician. Another attractive feature of the book is that a summary of important points, with commonsense advice for the reader to follow, is included in some of the clinical chapters. This reviewer found most of this information accurate and practical.

This book has the potential of being a widely read resource for many patients of all ages. It is important that the physician also review this material because it is often more comprehensive and complete than what we offer our patients in the office setting. Some physicians will recommend this book for their patients who have expressed concerns about aging in regard to themselves or their parents. It is an upbeat, positive, and sometimes humorous book that most people, including all *aging* physicians, will enjoy reading.

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HEAL THYSELF. THE HEALTH OF HEALTH CARE PROFESSIONALS

Edited by Cynthia D. Scott, PhD, and Joann Hawk, PhD. 335 pp, illustrated. New York, Brunner/Mazel Publishers, 1986. $30.00 (hardcover)

This book deals with the impairment of physicians and other health care professionals. It discusses the reasons leading to impairment as well as possible preventive educational measures. The editors are both PhDs, associated with the University of California and the Community Hospital in Santa Rosa, California, who have written extensively on the subject, often in collaboration with other experts. Many of the chapters contain extensive references. Thus the book is useful as a reference for much of the subject matter.

The book covers "burnout" and drug and alcohol abuse, as well as mental illness. Its contents are divided into the following sections: understanding impairment; interventions for prevention; and emergent strategies. The first section is perhaps the most valuable, especially the chapter by Nancy C. A. Roeske, MD, entitled, "Risk Factors and Predictable Hazards of a Health Care Career."

Although the majority of the authors hold PhD or MS degrees rather than

MDs, the latter have collaborated on a number of the chapters.

In general the book is concerned with causative "stress" factors and prevention. Intervention and treatment modalities are mentioned but not given major consideration. The changes suggested for reducing pressure on premedical, medical, and postgraduate students are well intended, but may not be easily accomplished.

Education at all levels is desirable, but its effectiveness for those out in the field is an open question. Nonetheless I fully support many of the preventive education programs mentioned. They should be encouraged. This is a good and worthwhile book in its field, whose editors have successfully met their objective.

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ANIMAL AGENTS AND VECTORS OF HUMAN DISEASE

Fifth Edition. Edited by Paul Chester Beaver, PhD, and Rodney Clifton Jung, MD. 281 pp, illustrated. Philadelphia, Lea & Febiger, 1985. $28.50 (hardcover)

This text revises the fourth edition by Faust, Beaver, and Jung published in 1975 and reprinted in 1976, 1979, 1980 and 1982. Its stated purpose is to cover knowledge of animals that cause or serve as vectors for organisms causing disease in humans. The text accomplishes this objective less well than the ninth edition of *Clinical Parasitology* by Beaver, Jung, and Cupp. However, as a text for medical students it is more than adequate, especially during a time of totally unwarranted de-emphasis on this increasingly important discipline in medical schools throughout the country. The authors and their many contributions to the field of parasitology are legendary.

Chapter numbers and titles are essentially unchanged from the previous edition, except that the final chapter, previously "Entomological Material, Intermediate and Reservoir Hosts," has been replaced by "Treatment for Parasitic Diseases." The book's five sections and 21 chapters have been streamlined and updated. While the same amount of text has been retained, it has been rearranged into columns rather than full pages.

The discussion of taxonomy has been updated and the section on classification removed from the introductory chapter. Many figures have been reduced in size to fit into single columns. Some of the old photos have been replaced, but not always with more instructive ones. Even where the same photos have been used, they are not always reproduced as well as in the previous edition. However, some of the older photographs are better reproduced in the new edition. Disappointingly few electron microscopy plates have been included, although numerous new and instructive histopathology plates are used.

Updated information on *Babesia*, *Giardia*, *Sarcocystis*, *Pneumocystis*, and the amphizoic *Naegleria*, *Acanthamoeba*, *Micronema* and *Pelodera* is included, as well as the recently discovered *Schistosoma mekongi*. *Dientamoeba fragilis* has been moved into its appropriate place as a trichomonad, and the section on *Leishmania* species has been expanded, as has that on *Dirofilaria*. The section on arthropods appears to have been shortened, but with the inclusion of additional and more instructive photographs.

Arthropods, molluscs, and vertebrate animals have been added to the chapter on "Diagnostic Materials and Methods" and *Pneumocystis*, perhaps prematurely, to the chapter on "Immunologic Diagnoses." It is gratifying to see the caveat that schistosomal immunologic tests are less than dependable.

The new fifth edition compares very favorably with the excellent fifth edition of Brown's *Basic Clinical Parasitology*, and has the obvious advantage of being two years newer. But however superior both may be for teaching medical students, neither text approximates the outstanding ninth edition of *Clinical Parasitology* for most other teaching purposes.

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POETRY AS HEALER. MENDING THE TROUBLED MIND

Edited by Jack J. Leedy, MD. 320 pp. New York, Vanguard Press, 1985. $14.95 (paperback)

Poetry has been used as part of a therapeutic milieu for centuries, going back to the time of the ancient Greek physicians. John Stewart Mill spoke of Wordsworth's poetry as medicine, not simply as metaphor, but in the same sense that Graves referred to a well-chosen anthology of poems as a "complete dispensary for the more common mental disorders that may be used as much for prevention as for cure."

This book brings together chapters by more than 20 physicians, psychologists, and educators who discuss various aspects of the therapeutic uses of poetry in a variety of clinical situations.

E. Mansell Patterson, Chairman of the Department of Psychiatry at Georgia Medical College, discusses the psychodynamics of poetry. He states that the use of poetry by patients may afford some of the most fundamental, far-reaching revelations of the self. Robert E. Jones, Professor of Psychiatry at Jefferson Medical College, presents a chapter on the treatment of the psychotic patient using poetry therapy. He also gives a historical perspective on the use of poetry in an inpatient psychiatric setting. (The oldest known poem written by a mental patient in an American hospital appears in a memorandum book written in 1822 by Samuel Coates, a manager of the Pennsylvania Hospital, the nation's oldest.) Bill J. Barkley, former chief clinical psychologist at the California Men's Colony, talks of his experience with the use of poetry in a correctional institution in a chapter on "poetry in a cage." In their chapter, "Opening New Worlds for the Deaf and Disturbed," Dr Lucien Buck, Professor of Psychology, and Dr Aaron Kramer, Professor of English at Dowling College, discuss the use of poetry in a school for the deaf, a community guidance center, and a school for emotionally disturbed children.

Other chapters include those by Jack J. Seedy, who writes on the "principles of poetry therapy," Morris Morrison, who writes about "poetry therapy with disturbed adolescents," and Dorothy Kubak, who writes on "poetry therapy in a 600 school."

The authors give examples of the use of poetry in various therapeutic settings (groups, counseling centers, therapists' offices, private hospitals, psychiatric hospital units). The chapters are generally presented in an interesting and informative fashion with a clear use of words. Various examples of poetry written both by acknowledged poets and by patients are presented in a manner that helps to add to the overall interest of the text, but for those physicians who have a need for strong

scientific data this book will probably not be fulfilling. Physicians who require factual data as proof of treatment success will find that this book has various shortcomings. Thus, those with a particular interest in poetry and its potential use as a mental health treatment modality will probably find this type of book of greater interest than their more scientific-minded colleagues. *Poetry as Healer* can give the reader the impetus to do more reading on what is often a stimulating subject.

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RADIOLOGY OF ADVERSE REACTIONS TO DRUGS AND TOXIC HAZARDS

By George Ansell, MD. 389 pp, illustrated. Rockville, Md, Aspen Publications, 1985. $40.00 (hardcover)

This volume is the second edition of a previous work by the author originally published in 1974. The newer volume is expanded and includes imaging techniques and updates brought on by new imaging technology. The work is a compendium, in a handy size and at an attractive price, of reactions to toxicological substances of many sorts. The work is extensively referenced, with nearly 1,200 works being neatly footnoted.

Organizationally, the book is divided into five sections by organ system, not by toxicologic agent. As a result, there is some small amount of repetition for some substances when a drug affects more than one. Unlike many radiologic works, the text is very liberally sprinkled with clinical facts and interesting anecdotes, and therefore makes somewhat more interesting reading than the average radiologic text. Because the author is English, a large number of the references are European, and for that reason the American reader will find some of the toxicologic references even more exotic.

Dr Ansell has attempted to and succeeded in presenting an international work that covers the more mundane substances such as steroids and drug addiction and touches on the sublime. For instance, there are interesting sections on paraquat, blackfat-smoker's lung, sansert, and, of course, Thorotrast.

The major criticism of the volume is that the reproductions of radiographs are perhaps not quite up to the level of quality the practicing radiologist may be accustomed to seeing in journals such as *Radiology* and the *American Journal of Roentgenology*, which have exceptionally good reproductions.

The work is directed to radiologists, especially those who may have an active role in emergency radiology, and to a lesser extent to clinicians with an interest in toxicology. It would make a handy reference book for most general radiologists at a very reasonable price, considering the prices of other texts in this field. It is not meant to be nor is it the most comprehensive work on toxicology as a whole.

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CLINICAL PSYCHIATRY

By Howard S. Sudak, MD. 481 pp. St Louis, Mo, Warren H. Green Inc, 1985. $55.00 (hardcover)

Howard S. Sudak and his colleagues on the psychiatry faculty of the Case Western Reserve School of Medicine wrote this book to teach psychiatry to their second year medical students. A textbook of only 481 pages would seem to have a great deal to offer students and other health care professionals since we lack a good compact and nonencyclopedic textbook that is easily portable and yet reliable. However, this book only modestly succeeds.

Psychodynamic Freudian psychology is not explained in detail, but it is still presented as the theoretical framework for understanding normal and abnormal mental behavior. Unfortunately, the beginning student learns some psychoanalytic jargon but is left without a clear grasp of such basic notions as the concept that all behavior is motivated and that motivations for the same behavior may be described on biological, psychological, and sociological levels.

Psychiatry has begun a move toward the scientific method and a closer connection with biology, medicine, and the social sciences. An extremely important concept for beginning students of psychiatry is that our thoughts, feelings, and actions make sense, even if only to ourselves, because they are adaptive and help us to cope with our situation. Searching through the index reveals no mention of such words as adaptation, coping, or even motivation. A greater emphasis on the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition (DSM III), categories of adjustment disorders, along with clinical examples of common reactions to pivotal events in the normal human life cycle, might have repaired this major weakness.

All of the major psychopathologic syndromes are presented briefly but well, and in the language of the 1980 DSM III. The logic and meaning of all five DSM III axes are not present. The second chapter entitled, "The Psychiatric Case Study," gives the misleading impression that a diagnostic assessment and treatment plan can rest on data from psychiatric history and mental status findings obtained from a one-to-one interview, and a general medical history and physical examination. It is not emphasized enough that both children and those adults functioning at a regressed level cannot provide reliable data for an interviewer to arrive at the essential inclusion or exclusion criteria on which a DSM III diagnosis may be based. Clinicians must rely on family or other reliable informants, on old medical records and contacts, and on the assistance of social workers and clinical psychologists. Nor is it evident that a DSM III diagnosis on all five axes still falls short of a diagnostic assessment on which a treatment plan may be based.

The public health relevance of the common psychiatric disorders is presented admirably well, and this is a major strength of the book. Some chapters such as the ones dealing with children, mental retardation, psychiatry and the law, and especially the several chapters on sexual behavior are much better done than others. On the whole we still await a good concise textbook on general psychiatry.

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Depression among elderly patients

Depression is a common illness among elderly patients, but it is often misdiagnosed, leading to ineffective forms of treatment. Dr Moonasar Rampertaap of Kansas City, Mo, in a recent issue of the *Southern Medical Journal* (1986; 79:1043–1044), described the successful alleviation of depressive symptoms in an elderly man that were caused by decreased oxygenation of the blood due to chronic obstructive pulmonary disease (COPD) and a sick sinus syndrome. The author stressed the importance of identifying physical disorders that can cause depression in older patients.

The patient was 71 years old and was taking bronchodilators for COPD. He had been admitted to the hospital four times in less than four months for symptoms suggestive of mental illness. These symptoms included suicidal behavior, insomnia, aggressive behavior, anorexia with weight loss, visual hallucinations, and disorientation. Psychological testing demonstrated that the patient was "anxious and depressed but not psychotic," and that he had a memory problem. During each of his four hospital stays, the patient was treated with a different drug, including flurazepam, doxepin, loxapine, and haloperidol–each providing some relief of specific symptoms.

During the fourth admission, an electroencephalogram—specifically the lead attached to the electrocardiogram—demonstrated occasional premature ventricular contractions. Subsequent 24-hour Holter monitoring led to the identification of tachycardia-bradycardia syndrome. Following implantation of a permanent pervenous pacemaker and initiation of antiarrhythmic therapy, the patient has remained without physical or psychological symptoms for two years.

The author cited studies that support an association between COPD and symptoms of depression, anxiety, irritability, and paranoia. He concluded that the COPD and sick sinus syndrome in this patient caused decreased oxygen saturation resulting in reduced brain perfusion, which may have accounted for his depressive symptoms.

Alzheimer's disease and previous psychiatric morbidity: A possible link

Dr M. O. Agbayewa conducted a study to test the hypothesis that there is "an association between earlier psychiatric illness and the development of Alzheimer's disease" (*J Am Geriatr Soc* 1986; 34:561–564).

In this retrospective investigation, the author reviewed the medical charts of 188 patients who were admitted to the hospital with a diagnosis of primary degenerative dementia, presenile dementia, or senile dementia. If the cause of the dementia could be identified or treated, the patient was excluded from the study. A control group, matched for age and sex, consisted of patients who had also been admitted to the medical or surgical wards of the hospital but who showed no signs of dementia. The charts were examined for evidence of previous functional psychiatric disorders that occurred before the age of 55 years.

Dr Agbayewa found a significant ($p < 0.001$) difference in the frequency of earlier psychiatric morbidity between patients with dementia ($^{34}/_{188}$) and the control population ($^{3}/_{80}$). The author proposed two possible explanations for this finding: The functional disorders are prodromal states of Alzheimer's disease; or previous psychiatric illness may signal an increased vulnerability to Alzheimer's disease.

The conclusion that "patients with Alzheimer's disease are more likely to have had a functional disorder earlier in life" raises the possibility of earlier diagnosis, and, perhaps, preventive therapy. The author stresses the shortcomings of retrospective studies and urges further research into the suggested link between previous psychiatric illness and the cognitive impairment associated with Alzheimer's disease.

Sense of control leads to improved health among the elderly

Recent research has strengthened the belief that a sense of control over one's fate may influence physical and mental health. This relationship between control and health has a special relevance in old age. Increasing age is often associated with a sense of loss of control—whether real or perceived—as one's physical and mental capabilities may decline and the decision making process may be arrogated by a younger relative, caretaker, or institution. In addition, the elderly must cope with the death of friends and family, the changes in lifestyle that accompany retirement, and the stereotyping about old age that can invoke feelings of incompetence and dependence.

In a recent article in *Science* (1986; 233:1271–1275), Judith Rodin describes studies suggesting that "the health of older people is strongly affected by control-enhancing interventions and control-restricting life circumstances." For example, involuntary relocation is a very stressful experience for an elderly person and can lead to increased morbidity and mortality. However, if the person believes that he can control and predict the change, he will be better able to manage the stress and will suffer less mental and physical trauma.

In institutions that care for the elderly, the personnel often reinforce dependent behavior and lack of control "in order to enhance patient manageability and treatability." This logic can actually prove harmful to patients; patients with no sense of control over their well-being may be less likely to try to prevent or overcome illness. Furthermore, studies have shown that persons who perceive a lack of control over their environment are more likely to characterize bodily sensations as symptoms of ill health.

Rodin reports several positive findings from control-enhancing intervention studies. "First, increased opportunities for control and a greater sense of personal efficacy can have a positive effect on the physical and psychological status of the institutionalized aged." And a study to discover whether restrictions in self-determination affect mental capabilities and the processing of information re-

NEWS BRIEFS are compiled and written by Vicki Glaser.

vealed that "enhanced control led to improvements in memory, satisfaction, and physical health."

Experimental drug shows promise against AIDS

Azidothymidine (AZT), an experimental drug with antiviral properties, has been shown to improve the health of patients with acquired immunodeficiency syndrome (AIDS) who have manifest specific symptoms of the disease. Preliminary studies with AZT suggest that the drug could prolong the lives of patients with *Pneumocystis carinii* pneumonia—a rare opportunistic infection associated with AIDS.

Burroughs Wellcome, the company that manufactures AZT, suspended testing of the drug when the favorable effects of AZT became apparent; it was considered unfair to continue giving placebos to the control population of patients with AIDS. During the three- to six-month study period, one of 145 patients taking AZT died, while 16 patients in the control group died, according to a September 19 report in the *New York Times*. AZT also resulted in fewer AIDS-related infections.

AZT, a drug initially synthesized to combat cancer, is believed to block the replication of the AIDS virus without killing the host cell. Although early tests demonstrated that high doses of the drug could damage bone marrow cells, this effect is not life threatening, and is overshadowed by the drug's ability to promote improved health and a stronger immune system. AZT is also able to penetrate the blood-brain barrier, an important quality of any anti-AIDS medication since the AIDS virus has been demonstrated in the central nervous system.

Federal health officials have stressed that the beneficial effects of AZT seem to be limited to a particular group of patients with AIDS. However, the success of AZT has sparked new hope for the development of an effective treatment, and possibly even a cure, for AIDS.

Research institute expands its goals

The Maimonides Research Institute in Haifa, Israel, serves as a repository of old writings and documents, specifically those of Rabbi Moses Ben Maimon (1135–1204), known as Maimonides. Maimonides was a physician and scholar. His writings, which focus on Jewish law and philosophy, contain valuable insights into the healing of both the mind and the body.

Maimonides is thought to have written 18 books on medicine, only seven of which have been published. Many other manuscripts have been preserved in libraries and private collections throughout the world. The institute aims to compile all of Maimonides' medical writings, and is organizing a cooperative program with physicians in many countries "for the purpose of applying Maimonidean law and medicine to modern medical practice." A building to house the institute is planned on Mount Carmel in Haifa.

Health benefits coalition formed

The newly formed New York State Public Sector Coalition on Health Benefits will have three major responsibilities: to serve as a clearinghouse for information concerning health insurance; to sponsor research on improving utilization and delivery of health care services; and to monitor the activities of hospitals and other providers of health care to ensure more cost-effective and efficient medical coverage. At the suggestion of Governor Mario Cuomo that a joint labor/management coalition on employee benefits be created, the Governor's Office of Employee Relations brought together seven representatives of public sector labor unions and seven members of state and local governments.

The coalition will collect information on cost containment techniques and the design of health insurance plans, and will study the utilization of health care based on geographic regions, the popularity of HMOs, and future needs in caring for the elderly. Labor unions represented on the coalition include the AFL-CIO, the teachers' union, the Civil Service Employees Association, the New York City Firefighters Association, and the unions of other public service employees.

Citizen action group fights drunk driving

RID (Remove Intoxicated Drivers)-USA is a nationwide citizen action group that campaigns against drunk driving. The group, established in Schenectady in 1978, is fighting for a national alcohol policy that would limit alcohol consumption through increased prices and taxation, require warning labels on all alcohol products, mandate a legal drinking age of 21 years, institute sobriety checkpoints, outlaw all-you-can-drink promotions, and prepare advertisements to counter those of the alcohol industry.

Specifically, RID is striving to reduce alcohol consumption among problem drinkers and among young people. The group faces stiff opposition from the alcohol industry, which would be threatened by a shrinking market. RID claims that the media has attempted to thwart its efforts by blocking the group's access to national television after it joined the SMART (Stop Marketing Alcohol on Radio and TV) campaign in 1983.

Among its projects, RID monitors court cases involving charges of driving while intoxicated, fights against weak judges and district attorneys, and lobbies for stronger reform laws. For more information contact RID, PO Box 520, Schenectady, NY 12301.

Treatment decision making for disabled neonates

The Executive Committee of the Medical Society of the State of New York recently adopted a position paper concerning treatment decision making for disabled neonates. This paper states:

A neonate born with a major malformation or who is critically ill for other reasons presents parents and physicians with agonizing decisions concerning the treatment of that infant. Parents or physicians might request the withholding or withdrawing of life sustaining care. The withholding of any type of treatment from a neonate because of a disability is ethically justified only when medical or surgical procedures are clearly futile and will only prolong the act of dying. In cases where it is uncertain whether treatment will be beneficial, treatment should not be withheld.

At the present time, it is difficult to identify a consensus on which infants with a broad range of congenital or acquired malformations should be treated. However, infants with conditions such as meningomyelocele and trisomy 21 should receive the benefit of medical and surgical treatment.

Attempts at simple solutions by the insistence that all infants be treated may not serve the interests of profoundly impaired neonates. The traditional method of a single physician making life-death judgments without involvement of other persons possessing additional facts, experience and points of view may lead to decisions that cannot be justified ethically.

The establishment of Infant Bioethics Review Committees to help the process of decision making for disabled neonates has been proposed by the American Academy of Pediatrics and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. The Medical Society of the State of New York believes that a well functioning and organized Review Committee is helpful in addressing such difficult ethical problems. Infant Bioethics Committees should have broad representation, and their recommendations should be based primarily on ethical rather than legal, economical or political considerations. Infant Bioethics Review Committees should not establish guilt or innocence, but should serve a positive function for neonates, families and professionals to make the decision making process more careful and critical and most likely to be justified ethically.

Council approves guidelines for caring for mentally impaired patients

At its meeting on June 26, 1986, the Council approved the following Guidelines for Physicians in the Medical Care of Their Mentally Impaired Patients in Residential Health Care Facilities. These guidelines were developed by the Committee on Aging and Nursing Homes.

GUIDELINES FOR PHYSICIANS IN MEDICAL CARE OF THEIR MENTALLY IMPAIRED PATIENTS IN RESIDENTIAL HEALTH CARE FACILITIES*

1. Definition:

For purposes of these guidelines, a mentally impaired patient is an individual whose cognitive abilities have been diminished by an organic psychotic condition† to the degree that the individual intellectually/cognitively cannot—

—understand and exercise rights that are reserved to the individual by custom and prevailing community standards as well as by law and regulation.

—comprehend the significance of medical information provided to the individual by the physician and the potential outcomes of medical care decisions as interpreted by the physician.

—make, or participate with the physician in making informed consent medical care decisions, whether such decisions that need to be made are at levels that are simple or complex, relatively insignificant or life-prolonging.

2. Need for *Guidelines* for physicians in caring for mentally impaired patients:

Among the nearly 100,000 patients/residents of Residential Health Care Facilities (RHCFs) in New York State, more than 50 percent are mentally impaired by organic psychotic disorders as well as physically impaired by chronic illnesses and other disabling conditions. In some RHCFs as many as 90 percent of patients/residents are moderately to severely impaired, intellectually/cognitively as well as physically dependent in some, many, or nearly all activities of daily living.

Mentally impaired patients/residents cannot participate meaningfully with physicians (and other health care workers) in exercising their rights, making informed consent decisions regarding day-to-day medical-clinical care, and accepting or rejecting life-prolonging treatments.

"Principles of Professional Conduct" of the Medical Society of the State of New York and the "Principles of Medical Ethics" of the American Medical Association set forth basic tenets that guide physician conduct of medical practice and relationships with patients. However, in physician care of RHCF patients/residents who are intellectually/cognitively impaired by mental impairment conditions, additional precepts and guidelines may be helpful, especially in those instances in which informed consent decision making is required and there is no duly empowered surrogate to participate with the physician in such decision making. The guidelines should help shape physician conduct and relationships, already in conformance with AMA and MSSNY principles, in such situations.

3. Principles/Guidelines:

The physician responsible for the care of a mentally impaired patient should:

1. Determine and document that the patient is cognitively impaired by one or more neurologically destructive disorders of the central nervous system.
2. Determine and document that the patient/resident cannot participate meaningfully with the physician in making medical-clinical care decisions that require informed consent.
3. Select and use, or direct the use of medical-clinical care measures that are specific for the patient's condition, intended to alleviate pain and suffering and otherwise designed for the benefit of the patient.
4. Protect the patient's rights, including those of informed consent by consulting whenever feasible, with a surrogate, if such has been appointed, or in the absence of such, by consulting or attempting to consult with the person or persons who will most closely approximate or reconstruct and

MEDICAL SOCIETY NEWS is compiled and written by Vicki Glaser.

* These guidelines are *not* intended for use by physicians in their medical management and decision making involving RHCF patients/residents who are not mentally impaired or whose apparent diminution in intellectual cognitive abilities may be attributable to pseudodementia, functional impairment or other conditions not included in the mentally impaired definition of these guidelines.

† "Organic Psychotic Disorder" is defined as a cognitively destructive disorder, usually progressive and irreversible, of the central nervous system and classifiable in code category No. 290 of the ICD-9-CM as a Senile or Presenile Organic Psychotic Condition (i.e., Senile or Presenile Dementia or related organic psychotic disorder) and also classifiable in code category No. 290 of the DSM-III as Primary Degenerative Dementia, Multi-infarct Dementia or a related Organic Mental Disorder.

represent the patient's pre-impairment views and decision-making wishes.

5. Assure that the medical-clinical care decision being sought is based primarily on medical-clinical needs and conditions of the patient and in keeping with currently acceptable standards of medical practice.

Journal ranks high among its peers

In a study undertaken by the Institute for Scientific Information (Philadelphia, Penn), 78 general and internal medicine journals were compared to determine their impact on the medical and research communities (*Ann Intern Med* 1986; 105:313–320). Ratings of the impact of various journals were based on citation analysis. Using data from the 1981 and 1982 *Journal Citation Reports*—a supplement to the *Science Citation Index*—the investigators determined the frequency with which items in these journals' 1980 and 1981 issues were cited.

The *New York State Journal of Medicine* ranked 29th in the number of citations received in 1981. *The Lancet* and the *New England Journal of Medicine*, respectively, led the list, claiming more than one third of all the 1981 citations for these 78 journals. The *British Medical Journal* and the *Journal of the American Medical Association* were ranked next, respectively, accounting for about 20% of all citations, followed by *Annals of Internal Medicine* and the *American Journal of Medicine*.

Dr Eugene Garfield, the author of the study, described the algorithm that was developed to weight specific characteristics of each journal item. The point system used enabled the identification of items that "contain substantive research whether they are letters, articles, or other material."

According to Dr Garfield, "the more frequently that a journal is cited, the more often the worldwide medical community indicates that journal's influence or impact." Examination of more recent data—through 1984—indicates no substantial changes in the rankings.

The *New York State Journal of Medicine* was the only state medical journal to make the list, and ranked well above the *Western Journal of Medicine*.

Close to 5,000 medical journals are published worldwide, of which approximately half are indexed in the *Index Medicus*. The *New York State Journal of Medicine* is among the 112 leading journals chosen by the *Index Medicus* from among approximately 2,500 journals for rapid monthly abridged indexing.

New York Medical Political Action Committee membership passes 5,000

Dr Edmond Gicewicz, Chairman, NYMPAC Board of Directors, announced that membership in the New York Medical Political Action Committee passed the 5,000 mark during 1986. Citing many factors, Dr Gicewicz, a practicing surgeon from Buffalo, NY, noted that a new sense of awareness has developed in the medical community. Legislation affecting physicians' economics, practice habits, and environment has created renewed concerns over physicians' rights, prerogative to practice, and a whole host of other issues.

In his years as a political activist, Gicewicz has sought to unite physicians and to use their force in the political arena. His efforts with NYMPAC have received the backing and support of the Medical Society of the State of New York and its leadership.

Headquarters Building of the Medical Society of the State of New York, Lake Success, New York

Dedicated December 10, 1971

OBITUARIES

In addition to these listings, the Journal *will publish obituaries written by physician readers. Inquiries should first be made to the Editor.*

Kyung Sup Ahn, MD, Staten Island. Died July 1986; age 51. Dr Ahn was a 1968 graduate of Soo Do Medical College (Seoul Women's Medical College). Dr Ahn was a member of the American Society of Anesthesiologists, Inc, the Richmond County Medical Society, and the Medical Society of the State of New York.

Robert Boyce Bryant, MD, Syracuse. Died August 28, 1986; age 71. Dr Bryant was a 1940 graduate of Cornell University Medical College, New York. He was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Surgery. Dr Bryant's memberships included the Academy of Medicine, the New York State Surgical Society, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Elliot T. Bush, MD, Elmira. Died August 28, 1986; age 70. He was a 1942 graduate of Temple University School of Medicine, Philadelphia. Dr Bush was a Fellow of the American College of Surgeons, a Diplomate of the American Board of Surgery, and a member of the Medical Society of the County of Chemung and the Medical Society of the State of New York.

Maurice Davidson, MD, Rochester. Died August 22, 1986, age 87. Dr Davidson was a 1925 graduate of Columbia University College of Physicians and Surgeons, New York. He was a member of the Academy of Medicine, the Medical Society of the County of Monroe, and the Medical Society of the State of New York.

Joseph A. D'Errico, MD, New Smyrna Beach, Florida. Died August 28, 1986; age 84. He was a 1927 graduate of Western Reserve University School of Medicine, Cleveland. Dr D'Errico was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Urology. His memberships included the Academy of Medicine, the American Urological Association, the Aerospace Medical Association, the American Geriatrics Society, the Medical Society of the County of Niagara, and the Medical Society of the State of New York.

Lewis Dickar, MD, Bayport. Died August 20, 1986; age 82. He was a 1930 graduate of Yale University School of Medicine, New Haven. Dr Dickar was a Fellow of the American College of Physicians, a Diplomate of the American Board of Physical Medicine and Rehabilitation, and a member of the American Academy of Physical Medicine and Rehabilitation, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

William Leonard Dorr, MD, Auburn. Died August 27, 1986; age 79. Dr Dorr was a 1936 graduate of the University of Rochester School of Medicine and Dentistry. He was a Fellow of the American College of Surgeons and a member of the Medical Society of the County of Cayuga and the Medical Society of the State of New York.

Benjamin Effron, MD, Palm Beach, Florida. Died January 1986; age 75. Dr Effron was a 1937 graduate of New York University College of Medicine, New York. He was a member of the Dutchess County Medical Society and the Medical Society of the State of New York.

Michael A. Ferragamo, MD, Floral Park. Died September 14, 1986; age 84. He was a 1927 graduate of the State University of New York Downstate Medical Center, New York. Dr Ferragamo was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Urology. His memberships included the American Urological Association, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Emanuel E. Feuer, MD, Hyde Park. Died October 18, 1985; age 77. Dr Feuer was a 1938 graduate of Universita Komenského Fakulta Lekárska Bratislave. He was a member of the American Psychiatric Association, the Dutchess County Medical Society, and the Medical Society of the State of New York.

Dennis Joseph Fiorentino, MD, Brooklyn. Died September 10, 1986; age 69. Dr Fiorentino was a 1942 graduate of State University of New York Downstate Medical Center, New York. Dr Fiorentino was a Fellow of the American College of Surgeons and a Diplomate of the American Board of Surgery. His memberships included the American Academy of Compensation Medicine, Inc, the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

Donato Peter Fischetti, MD, Boca Raton, Florida. Died September 11, 1986; age 73. He was a 1938 graduate of State University of New York Downstate Medical Center, New York. Dr Fischetti was a member of the American Geriatrics Society, the Medical Society of the County of Kings, and the Medical Society of the State of New York.

John Russell Jaicks, MD, Bronx. Died July 21, 1986; age 55. He was a 1956 graduate of Georgetown University School of Medicine, Washington, DC. Dr Jaicks was a Diplomate of the American Board of Obstetrics and Gynecology and a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Herman H. Janes, MD, Southport, Connecticut. Died August 13, 1986; age 94. Dr Janes was a 1917 graduate of Fordham University School of Medicine, New York. He was a Fellow of the American College of Surgeons and a member of the Bronx County Medical Society and the Medical Society of the State of New York.

Aloysius A. Kalinowski, MD, Buffalo. Died August 17, 1986; age 70. He was a 1942 graduate of the University of Buffalo School of Medicine. Dr Kalinowski

was a Diplomate of the American Board of Pediatrics and a member of the Medical Society of the County of Erie and the Medical Society of the State of New York.

Abraham Kosseff, MD, Rhinebeck. Age 95. Dr Kosseff was a 1915 graduate of State University of New York Downstate Medical Center, New York. He was a member of the Dutchess County Medical Society and the Medical Society of the State of New York.

Alfred Lapin, MD, Flushing. Died September 2, 1986; age 65. He was a 1953 graduate of the University of Pennsylvania School of Medicine, Philadelphia. Dr Lapin was a Fellow of the American College of Obstetricians and Gynecologists and the American College of Surgeons and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the American Society of Abdominal Surgeons, the Medical Society of the County of Queens, and the Medical Society of the State of New York.

Lawrence Lercher, MD, New York. Died March, 6, 1986; age 77. Dr Lercher was a 1934 graduate of State University of New York Downstate Medical Center, New York. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Benjamin Lewis, MD, Binghamton. Died August 30, 1986; age 74. Dr Lewis was a 1938 graduate of State University of New York Upstate Medical Center, Syracuse. He was a member of the Broome County Medical Society and the Medical Society of the State of New York.

Ben Garrison Lipton, MD, New York. Died July 26, 1986; age 89. He was a 1925 graduate of St Louis University School of Medicine. Dr Lipton was a member of the New York County Medical Society and the Medical Society of the State of New York.

James Emerson Macaluso, MD, Lockport. Died August 21, 1986; age 66. Dr Macaluso was a 1944 graduate of the University of Buffalo School of Medicine. He was a member of the Academy of Medicine, the Medical Society of the County of Niagara, and the Medical Society of the State of New York.

John A. Manganelli, MD, Utica. Died August 29, 1986; age 64. He was a 1945 graduate of State University of New York Upstate Medical Center, Syracuse. Dr Manganelli was a member of the Medical Society of the County of Oneida and the Medical Society of the State of New York.

James A. McCullough, MD, Black River. Died September 10, 1986; age 81. Dr McCullough was a 1930 graduate of Queens University Faculty of Medicine, Kingston. He was a member of the Medical Society of the County of Jefferson and the Medical Society of the State of New York.

Joseph P. Ostrowski, MD, Salem, South Carolina. Died August 29, 1986; age 68. Dr Ostrowski was a 1943 graduate of Hahnemann Medical College and Hospital of Philadelphia. He was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Orthopedic Surgery. Dr Ostrowski was a member of the American Academy of Orthopaedic Surgeons, the Pan American Medical Association, the Medical Society of the County of Oneida, and the Medical Society of the State of New York.

Orra Almira Phelps, MD, Saratoga Springs. Died August 26, 1986; age 91. Dr Phelps was a 1927 graduate of Johns Hopkins University School of Medicine, Baltimore. Dr Phelps was a member of the Medical Society of the County of Saratoga and the Medical Society of the State of New York.

Thaddeus T. Przybycien, MD, Buffalo. Died August 14, 1986; age 79. Dr Przybycien was a 1933 graduate of the University of Buffalo School of Medicine. Dr Przybycien was a member of the American Geriatrics Society, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Steven Rich, MD, Sun City, Arizona. Died August 27, 1986; age 77. He was a 1938 graduate of Karl-Franzens-Universität Medizinische Fakultät, Graz, Germany. Dr Rich was a member of the American Academy of Family Practice, the Medical Society of the County of Rockland, and the Medical Society of the State of New York.

Robert Rivkin, MD, Bal Harbour, Florida. Died July 13, 1986; age 88. Dr Rivkin was a 1921 graduate of State University of New York Downstate Medical Center, New York. He was a member of the Medical Society of the County of Kings and the Medical Society of the State of New York.

George William Rogers, MD, New York. Died September 18, 1986; age 67. He was a 1943 graduate of Emory University School of Medicine, Atlanta. Dr Rogers was a member of the Academy of Medicine, the American Academy of Family Practice, the American Academy of Occupational Medicine, the Suffolk County Medical Society, and the Medical Society of the State of New York.

Joseph Francis Rooney, MD, Manhasset. Died August 31, 1986; age 78. He was a 1934 graduate of Johns Hopkins University School of Medicine, Baltimore. Dr Rooney was a Fellow of the American College of Surgeons, a Qualified Fellow of the International College of Surgeons, and a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the New York County Medical Society and the Medical Society of the State of New York.

Max Ira Roven, MD, New York. Died December 31, 1985; age 96. Dr Roven was a 1914 graduate of Fordham University School of Medicine, New York. He was a member of the New York County Medical Society and the Medical Society of the State of New York.

Thomas Joseph Serio, MD, Buffalo. Died August 31, 1986; age 88. Dr Serio was a 1928 graduate of Stritch School of Medicine of Loyola University, Chicago. He was a member of the Medical Society of the County of Erie and the Medical Society of the State of New York.

Carl Benton Smith, MD, Naples, Florida. Died August 15, 1986; age 77. He was a 1936 graduate of State University of New York Upstate Medical Center, Syracuse. Dr Smith was a Diplomate of the American Board of Radiology and a member of the Ontario County Medical Society and the Medical Society of the State of New York.

John D. Van Zandt, MD, Tuxedo Park. Died September 3, 1986; age 71. Dr Van Zandt was a 1941 graduate of New York University College of Medicine, New York. He was a Fellow of the

American Academy of Family Practice and a member of the Medical Society of the County of Orange and the Medical Society of the State of New York.

Julius Voehl, MD, Syracuse. Died August 18, 1986; age 90. He was a 1921 graduate of Hessische Ludwigs-University Medizinische Fakultät, Giessen, Hessen, Germany. Dr Voehl was a member of the Academy of Medicine, the American Academy of Dermatology, the Onondaga County Medical Society, and the Medical Society of the State of New York.

Jacob J. Wechsler, MD, New York. Died September 16, 1986; age 86. Dr Wechsler was a 1925 graduate of McGill University Faculty of Medicine, Montreal. He was a member of the American Academy of Family Practice, the Bronx County Medical Society, and the Medical Society of the State of New York.

Jane Carroll Brady Wiles, MD, Grand Island. Died August 28, 1986; age 66. Dr Wiles was a 1945 graduate of the University of Buffalo School of Medicine. Dr Wiles was a member of the American Medical Women's Association, the American Public Health Association, the Medical Society of the County of Erie, and the Medical Society of the State of New York.

Frank Vincent Yannelli, MD, Baldwin. Died September 21, 1986; age 82. He was a 1928 graduate of State University of New York Downstate Medical Center, New York. Dr Yannelli was a Fellow of the American Academy of Family Practice and a member of the Nassau County Medical Society and the Medical Society of the State of New York.

ERRATUM

Based on information provided by the Medical Society of the County of Kings, the November 1986 issue of the *Journal* erroneously reported the death of John Joseph Pellegrini, MD, of Brooklyn. Dr Pellegrini is alive and well and in active practice in Brooklyn.

Guidelines for authors

Originality

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media, and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1983; 83:1089–1094). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal*'s particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

Preparation

An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

Categories

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with Système Internationale (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

Figures

The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

References

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

References should be indicated in the text by superscript numbers following the name of the author (eg, Smith[2] reported two cases).

The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear in the text. When there are three or fewer authors, all should be listed; where there are four or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Sample references:

1. Kepes ER, Thomas P, Vemulapalli K: Methadone and intravenous morphine requirements. *NY State J Med* 1983; 83: 925–927.
2. Behrman RE, Vaughn VC: *Nelson Textbook of Pediatrics*, ed 12. Philadelphia, WB Saunders Co, 1983, pp 337–338.

Review

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

Address correspondence to Pascal James Imperato, MD, Editor, *New York State Journal of Medicine*, P.O. Box 5404, 420 Lakeville Road, Lake Success, NY 11042.

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CLASSIFICATION CODES

CC = Clinical Conference
CPC = Clinicopathologic Conference
CR = Case Report
ED = Editorial Commentary
EP = Essay in Pediatrics
HIST = History of Medicine
LE = Letter to the Editor
NF = News Feature
RPC = Correlation Conference in Radiology and Pathology

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COURTESY N.Y. CONVENTION & VISITORS BUREAU

Medical Society of the State of New York

ANNUAL CME ASSEMBLY

Clinical Dilemmas & Controversies

March 13–15, 1987

and the

Annual Meeting of the House of Delegates

March 12–15, 1987

The New York Hilton
New York City

HIGHLIGHTS . . .

- 22 Sessions
- Panel Discussions
- Technical Exhibits
- Two Receptions
- President's Reception & Dinner Dance

CLIP & MAIL

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NAME _____ TITLE _____

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STREET _____

CITY/STATE/ZIP _____

REMARKS _____

(please print)

NOTE: Reservations must be received no later than February 19, 1987 and will be held only until 6 p.m. on day of arrival unless later hour is specified.

please print

ARRIVAL DATE _____

☐ 2-4 p.m. ☐ 4-6 p.m. ☐ 6-8 p.m. ☐ after 8 p.m.

DEPARTURE DATE _____

(checkout time is 1 p.m.)

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MEDICAL SOCIETY OF THE STATE OF NEW YORK
Annual Meeting of the House of Delegates
March 12–15, 1987
Annual CME Assembly
March 13–15, 1987

Circle Preferred rate:

Singles:	$130	$145	$155
Doubles/Twins:	$155	$170	$180
Executive Tower:	$200 Single/Double		
Suites: (P&1):	$360	$395	
Suites: (P&2):	$460	$495	

Rates subject to 8¼% N.Y. State sales tax; $2.00 per room per night, and 5% N.Y.C. occupancy taxes. (If room at the rate requested is unavailable, one at the nearest available rate will be reserved.)

GENERAL INFORMATION

All physicians, members of the allied professions, and their guests are invited to attend the Medical Society of the State of New York's Annual CME Assembly to be held March 13–15, 1987, at the New York Hilton. The two and one-half days of meetings will provide the individual physician with a possible 18 credits out of a total of 93 Category 1, CME credit hours being offered. The Medical Society of the State of New York is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for physicians. Over 125 outstanding speakers, including a number from out-of-state, will present papers at 20 sessions.

The theme of the CME Sessions will be "Clinical Dilemmas and Controversies." A few of the subjects to be presented will be, Terrorism & Medicine; Computers in Medicine; AIDS in Pregnancy; Humanism and Medical Ethics in Our Technological Age; Intensive Care for AIDS Victims; Thoracic Aortic Balloon Occlusion: Methods and Indications; and the Role of the Physician as the Patient's Advocate. For details, see the Preliminary Program which appears in the December 1986 issue of the *New York State Journal of Medicine.* Our program will offer the clinician timely approaches in diagnosis and treatment of diseases in a wide range of medical specialties.

Here are comments from some of the attendees at the 1986 CME Assembly: "The sessions were educational, and the topics were timely," "There was an excellent choice of qualified speakers," "I found the material was practical, concise and clinically useful." Don't miss this opportunity to gain category 1 credits over a weekend when you are free from office hours. Also, bring your family to New York City to enjoy the sights. There is no registration fee for MSSNY members or members of any other state medical society.

Professional representatives from more than 60 companies will be in the Rhinelander Gallery Exhibit Hall on Friday and Saturday to discuss their products and services. The Technical exhibits will include drug products, office management systems, medical and surgical suppliers, health insurance plans, pension plans and more.

SPECIAL EVENTS

Thursday, March 12

The Annual Dinner Dance, in honor of our President, John Finkbeiner, M.D., will be held in the Trianon Ballroom of the New York Hilton. The reception will be held in the Mercury Ballroom starting at 7:00 p.m. All attendees are welcome. Tickets are $75.00 per person and should be ordered in advance from the Medical Society.

UNITED NATIONS HEADQUARTERS
— Courtesy N.Y. Convention & Visitors Bureau

Friday, March 13 and Saturday, March 14

A reception for physicians, their guests, the allied professions and exhibitors will be held both days in the Exhibit Hall between 5:00 p.m. and 6:00 p.m. A free drawing for a color TV set will take place at both receptions.

HOTEL RESERVATIONS

Physicians must make their own reservations with the New York Hilton no later than February 19, 1987. After that date, rooms are on an availability basis only. If making reservations by telephone, please mention that you are attending the Medical Society Convention for billing at the special rate.

SIGHTSEEING

A partial check list of the sights New York City has to offer

- ☐ American Museum of Natural History and Naturemax Theatre
- ☐ Chinatown
- ☐ Citicorp Center
- ☐ Frick Collection of paintings; sculpture; etc.
- ☐ Gray Line Sightseeing—conducted tours via Motorcoach
- ☐ Greenwich Village
- ☐ Hayden Planetarium
- ☐ Lincoln Center for the Performing Arts
- ☐ Metropolitan Museum of Art
- ☐ Museum of Modern Art
- ☐ New York Stock Exchange
- ☐ Radio City Entertainment Center
- ☐ Rockefeller Center
- ☐ South Street Seaport
- ☐ Staten Island Ferry
- ☐ Theatre Museum
- ☐ Trump Tower
- ☐ United Nations Headquarters
- ☐ World Trade Center
- ☐ WW II Aircraft Carrier Intrepid

1987
PRELIMINARY PROGRAM
Annual CME Assembly
March 13-15, 1987

Annual Meeting of the
House of Delegates
March 12-15, 1987

The New York Hilton
New York City

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REGISTRATION & MEETING HOURS

CME Assembly

Registration is open to MSSNY members, spouses, invited guests, non-member physicians, and members of the allied professions. There is no registration fee for MSSNY members, members of other state medical societies, residents/interns, speakers, medical students, medical assistants, and spouses. There is a registration fee for non-member physicians—$50; and allied professions—$10.

An advance registration form will be found in this section. For those who register in advance, your identification badge will be held at the CME Registration Desk located in the Rhinelander Gallery Exhibit Hall on the second floor of the hotel. For those who have not registered in advance, registration will take place on Friday, March 13, from 8:00 a.m. to 5:00 p.m., and Saturday, March 14, from 8:30 a.m. to 5:00 p.m., and on Sunday, March 15, from 8:30 a.m. to 12:30 p.m.

All registrants are required to show identification at the registration desk before a badge is issued. Identification badges are required for admittance to all CME Meetings and exhibits.

CME meeting hours will be on Friday, March 13, from 9:00 a.m.–12:30 p.m., and from 2:00 p.m. to 5:00 p.m., and Saturday, March 14, from 10:00 a.m. to 1:00 p.m. and from 2:00 p.m. to 5:00 p.m., and on Sunday, March 15, from 10:00 a.m. to 1:00 p.m.

Delegates

Registration for delegates will take place on the second and third floor Promenades as follows: Wednesday, March 11 from 12 Noon to 6:00 p.m.; Thursday, March 12, Friday, March 13, and Saturday, March 14, from 8:30 a.m. to 5:30 p.m.; and Sunday, March 15, from 8:30 a.m. to 12 Noon.

The 181st Annual Meeting of the House of Delegates will be called to order at 1:00 p.m. on Thursday, March 12, 1987 in the East Ballroom of the New York Hilton. The schedule follows: Thursday, March 12 from 1:00 p.m. to 5:00 p.m.; Saturday, March 14 from 9:00 a.m.–5:30 p.m.; and on Sunday, March 15 from 9:00 a.m. to 1:00 p.m. (8:00 a.m.–2:00 p.m. if necessary).

AUXILIARY TO MSSNY

The Auxiliary House of Delegates meeting will take place on Friday, March 13 from 9:00 a.m.–4:00 p.m., and on Saturday, March 14 from 9:00 a.m.–12 Noon in the Mercury Ballroom of the New York Hilton.

CME CREDITS

The Medical Society of the State of New York is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for physicians. The Medical Society of the State of New York designates all CME activities in this CME Assembly as meeting the criteria for Category 1.

Each program is acceptable for prescribed or elective credits by the American Academy of Family Physicians (AAFP) as designated. The Medical Society's CME credit forms will be issued at the entrance to each meeting room at the opening of each session.

EXHIBITS

Technical exhibits will be located in the Rhinelander Gallery on the second floor of the New York Hilton. Exhibits will be on view Friday, March 13 and Saturday, March 14 from 9:00 a.m. to 6:00 p.m.

PHYSICIAN MESSAGE CENTER

Messages for the physicians attending the CME sessions may be left at the MSSNY Information Desk located in the Exhibit Hall on the second floor. Messages for Delegates may be left at the Delegates Information Desk on the third floor, West Promenade. The New York Hilton telephone number is 212-586-7000.

COFFEE BREAKS

Coffee, sponsored by the Medical Society of the State of New York, will be served in the Exhibit Hall on the second floor daily from 9:00 a.m. to 5:00 p.m. All registered attendees are welcome.

DINNER DANCE

On Thursday, March 12, the Annual Dinner Dance will be held in the Trianon Ballroom, preceded by a reception in the Mercury Ballroom at 7:00 p.m. Tickets should be ordered in advance from the Medical Society of the State of New York. Subscription is $75.00 per person. See the order form in this section.

RECEPTION

A reception, sponsored by the MSSNY, will be held on Friday, March 13 and Saturday, March 14 from 5:00 p.m. to 6:00 p.m. in the Rhinelander Gallery Exhibit Hall located on the second floor of the hotel. All physicians, their spouses, the allied professions and exhibitors are welcome. A free drawing for a color TV will be held at both receptions.

1987 ANNUAL CME ASSEMBLY

Medical Society of the State of New York
The New York Hilton, New York City

Clinical Dilemmas and Controversies

FRIDAY, MARCH 13

9:00 a.m. - 1:00 p.m. General Session: Clinical and Ethical Dilemmas, *Gramercy A & B*

2:00 p.m. - 5:00 p.m.
Chest Diseases, *Regent Parlor*
Cardiovascular Diseases, *Murray Hill B*
Pediatrics/Orthopedic Surgery, *Murray Hill A*
Neurology/Alcoholism/Physical Medicine & Rehabilitation, *Nassau A*
Emergency Medicine/Critical Care/Otolaryngology, *Gramercy B*
Medical Liability, *Gramercy A*

SATURDAY, MARCH 14

10:00 a.m. - 1:00 p.m.
Internal Medicine (All Day), *Regent Parlor*
Ophthalmology (All Day), *Sutton Parlor Center*
Psychiatry (All Day), *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation (All Day), *Murray Hill A*
Urology/Pathology, *Nassau A*
Dermatology, *Nassau B*

2:00 p.m. - 5:00 p.m.
Internal Medicine, *Regent Parlor*
Ophthalmology, *Sutton Parlor Center*
Psychiatry, *Murray Hill B*
Hand Surgery/Orthopedic Surgery/Physical Medicine & Rehabilitation, *Murray Hill A*
Computers in Medicine, *Madison Suite*
Terrorism and Medicine, *Sutton Parlor South*

SUNDAY, MARCH 15

10:00 a.m. - 1:00 p.m.
Allergy and Immunology, *Murray Hill B*
General Surgery/Radiology/Anesthesiology, *Murray Hill A*
Obstetrics and Gynecology/Women's Medical Society of New York State, *Gramercy B*
Family Practice/Orthopedic Surgery, *Nassau A*
Neurosurgery, *Morgan Suite*

CME CREDITS: Each program will be eligible for CME Category 1 credits on an hour-for-hour basis. The Medical Society of the State of New York is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for physicians.

Technical Exhibits

1987 ANNUAL CME ASSEMBLY

SCIENTIFIC PROGRAM COMMITTEE

STEPHEN NORDLICHT, M.D., New York City, Chairman
PETER B. FARNSWORTH, M.D., Lake Success, Director, Division of Scientific Activities

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Anesthesiology

KENNETH FREESE, M.D., East Meadow
New York State Society of Anesthesiologists

Cardiovascular Diseases

MOHAMMAD ZAHIR, M.D., Brooklyn
New York Cardiological Society

Chest Diseases

J. RICHARD TYNER, M.D., Clifton Springs
American College of Chest Physicians

Dermatology

EUGENE BODIAN, M.D., Great Neck
New York Society of Dermatology

Emergency Medicine

LORRAINE GIORDANO, M.D., Jamaica
New York Chapter of American College of Emergency Physicians

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Internal Medicine

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New York State Society of Internal Medicine

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American College of Obstetricians and Gynecologists District II

Occupational & Environmental Health including Workers' Compensation

GOTTFRIED F. H. LEHMANN, M.D., Jamaica

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SAMUEL PACKER, M.D., Manhasset
New York State Ophthalmological Society

Orthopedic Surgery

DAVID HIRSH, M.D., Scarsdale
New York Society of Orthopedic Surgery

Otolaryngology

STEVEN PARNES, M.D., Albany
New York State Society of Otolaryngology—Head and Neck Surgery

Pathology

NATHAN S. TAYLOR, M.D., Rochester
New York Society of Pathology

Pediatrics

MARVIN BLUMBERG, M.D., Jamaica
American Academy of Pediatrics, District 11

Physical Medicine and Rehabilitation

SAMUEL SVERDLIK, M.D., New York City
New York Society of Physical Medicine and Rehabilitation

Psychiatry

RICHARD B. DROOZ, M.D., New York City
New York State Psychiatric Association

Radiology

RITA GIROLAMO, M.D., Valhalla
New York State Chapter of the American College of Radiology

Surgery

LESLIE WISE, M.D., New Hyde Park
New York State Society of Surgeons

Urology

MARCUS SHOOBE, M.D., Albany
New York State Urological Society

Women's Medical Society of New York State

PATRICIA NUMANN, M.D., Syracuse
New York State Women's Medical Society

FRIDAY, MARCH 13, 1987

PLENARY SESSION

9:15 A.M.–12:30 P.M.
GRAMERCY A & B

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CLINICAL AND ETHICAL DILEMMAS OF MEDICINE TODAY

GEORGE J. LAWRENCE, JR., M.D., Glen Cove, *Moderator*

Executive Vice President Emeritus, Medical Society of the State of New York

Objective: This conference has been planned with the purpose of presenting to physicians the increasing changes in the practice of medicine. Focus will be on the clinical and ethical aspects and the demands which have to be met with new insights.

9:15 A.M. **Introduction**

STEPHEN NORDLICHT, M.D., New York City

Chairman, Scientific Program Committee, Medical Society of the State of New York

9:30 A.M. **Clinical Privileges: Self Interest and Professional Ethics**

JOHN R. BALL, M.D., J.D., Philadelphia, Pennsylvania

Executive Vice President, American College of Physicians

9:50 A.M. **Developing an Awareness of Ethical Issues and Values in Medical Students**

THOMAS H. MEIKLE, M.D., New York City

The Stephen & Suzanne Weiss Dean, Cornell University Medical College; Provost for Medical Affairs, Cornell University

10:10 A.M. **Humanism and Medical Ethics in Our Technological Age**

STEPHEN NORDLICHT, M.D., New York City

Consulting Psychiatrist, Memorial Sloan Kettering Cancer Center, Cornell University Medical College

10:30 A.M. **Questions and Answers**

10:50 A.M. **The Morality of Hospital Stewardship**

WILLIAM D. SHARPE, M.D., New York City

Director of Laboratories, Cabrini Medical Center

11:10 A.M. **The Role of the Physician as the Patient's Advocate**

LEON J. WARSHAW, M.D., New York City

Executive Director, New York Business Group on Health; Clinical Professor of Environmental Medicine, New York University School of Medicine

11:30 A.M. **The Basic Ethical Imperative of the Physician**

CARLETON B. CHAPMAN, M.D., Hanover, New Hampshire

Professor Emeritus of the History and Philosophy of Medicine, Albert Einstein College of Medicine of Yeshiva University

11:50 A.M.–12:30 P.M. **Questions and Answers**

Chest Diseases
Joint Meeting With
American College of Chest Physicians

2:00 P.M.–5:00 P.M.
REGENT PARLOR

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

SOME INTERESTING CONTROVERSIES IN PULMONARY MEDICINE

J. RICHARD TYNER, M.D., F.C.C.P., Clifton Springs, *Moderator*

Director, Pulmonary Unit, Clifton Springs Hospital; President, New York State Chapter American College of Chest Physicians

Objective: To air several recently studied clinical problems relevant to chest medicine and surgery.

2:00 P.M. **Respiratory Hazards in New York State: How Safe Is It Down on the Farm?**

JOHN J. MAY, M.D., F.C.C.P., Cooperstown

Attending Physician, Mary Imogene Bassett Hospital; Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons

2:40 P.M. **THE 36th HOWARD LILIENTHAL MEMORIAL LECTURE: Physiological Exercise Testing: What Can It Do For You?**

(continued)

DAVID J. KANAREK, M.D., M.B., B.Ch., F.C.C.P., Boston, Massachusetts

Associate Clinical Professor of Medicine, Harvard Medical School; Director, Cardiopulmonary Exercise Laboratory, Massachusetts General Hospital

3:30 P.M. Controversies in Indoor and Outdoor Air Pollution

DOUGLAS DOCKERY, Ph.D., Boston, Massachusetts

Research Assistant in Respiratory Epidemiology, Department of Environmental Science and Physiology, Harvard School of Public Health

4:15 P.M.–5:00 P.M. A Clinical Dilemma: Management of the Pancoast Tumor

RICHARD H. FEINS, M.D., F.C.C.P., Rochester

Attending Surgeon, Cardiothoracic Surgery, Rochester General Hospital

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Cardiovascular Diseases
Joint Meeting With
The New York Cardiological Society

2:00 P.M.–5:00 P.M.
MURRAY HILL B

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CONTROVERSIES IN CARDIOLOGY

ALAN F. LYON, M.D., Brooklyn, *Moderator*

Director of Medicine, Brookdale Hospital Medical Center; Professor of Medicine, State University of New York Health Sciences Center at Brooklyn

Objective: To bring audience up to date on the diversity of opinion in two areas of controversy in cardiology: (1) does silent ischemia require treatment; (2) should all patients without specific contraindications have coronary arteriography after acute myocardial infarction.

2:00 P.M. Should Silent Ischemia, Once Identified, Be Treated: Pro

PETER COHEN, M.D., Stony Brook

Professor of Medicine; Chief of Cardiology, State University of New York at Stony Brook Health Sciences Center

2:30 P.M. Should Silent Ischemia, Once Identified, Be Treated: Con

EDGAR LICHSTEIN, M.D., Brooklyn

Chief, Cardiology, Maimonides Medical Center; Professor of Medicine, State University of New York Health Sciences Center at Brooklyn

3:00 P.M. Discussion Period

3:30 P.M. Should All Patients With Recent Myocardial Infarction and Without Specific Contraindication, Undergo Coronary Arteriography: Pro

HARVEY KEMP, M.D., New York City

Director, Cardiology, St. Luke's-Roosevelt Hospital Center; Professor of Medicine, Columbia University College of Physicians and Surgeons

4:00 P.M. Should All Patients With Recent Myocardial Infarction and Without Specific Contraindication, Undergo Coronary Arteriography: Con

SIDNEY GOTTLIEB, M.D., Baltimore, Maryland

Director, Cardiac Catheterization Laboratory, Francis Scott Key Medical Center; Assistant Professor of Medicine, Johns Hopkins University School of Medicine

4:30 P.M.–5:00 P.M. Discussion Period

Pediatrics/Orthopedic Surgery
Joint Meeting With
American Academy of Pediatrics District II/New York Society of Orthopedic Surgery

2:00 P.M.–5:00 P.M.
MURRAY HILL A

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

STRUCTURAL AND FUNCTIONAL DISORDERS IN CHILDREN

MARVIN L. BLUMBERG, M.D., Jamaica, *Moderator*

Chairman, Department of Pediatrics, Jamaica Hospital; Associate Professor of Clinical Pediatrics, School of Medicine, State University of New York at Stony Brook

(continued)

Objective: To enable the professional involved with children to recognize, diagnose and manage anatomic and functional disorders and disabilities.

2:00 P.M. Differential Diagnosis of the Infant with Cerebral Palsy

ALFRED L. SCHERZER, M.D., Riverhead

Attending Pediatrician, New York Hospital; President, American Academy for Cerebral Palsy and Developmental Medicine

2:30 P.M. Questions and Answers

2:45 P.M. Adrenocortical Disorders in Children and Their Manifestations

CHHAYA CHAKRABARTI, M.D., Richmond Hill

Clinical Assistant Professor of Pediatrics, Columbia Presbyterian Medical Center; Attending Pediatrician, Jamaica Hospital

3:15 P.M. Questions and Answers

DAVID M. HIRSH, M.D., Bronx, *Moderator*

Staff, Orthopedic Surgery, Albert Einstein College of Medicine of Yeshiva University; Associate, Orthopedic Surgery, Bronx Municipal Hospital Center and Bronx-Lebanon Hospital Center

3:30 P.M. Scoliosis for the Pediatrician: Practical Considerations for Office Practice

STANLEY HOPPENFELD, M.D., Bronx

Associate Clinical Professor of Orthopedic Surgery, Albert Einstein College of Medicine of Yeshiva University; Attending Orthopedic Surgeon, Hospital for Joint Diseases Orthopedic Institute

4:00 P.M. Questions and Answers

4:15 P.M. Congenital Hip Dislocation: An Overview

LEONARD P. SEIMON, M.D., Bronx

Professor of Orthopedic Surgery, Albert Einstein College of Medicine of Yeshiva University; Director, Pediatric Orthopedic Service, Montefiore Hospital and Medical Center

4:45 P.M.–5:00 P.M. Questions and Answers

Neurology/Alcoholism/Physical Medicine & Rehabilitation
Joint Meeting With
American Medical Society on Alcoholism—New York Chapter
New York Society of Physical Medicine & Rehabilitation

2:00 P.M.–5:00 P.M.
NASSAU A

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

MEDICINE AND THE ADDICTIVE SOCIETY

SAMUEL SVERDLIK, M.D., New York City, *Moderator*

Director, Rehabilitation Medicine, St. Vincent's Hospital and Medical Center of New York; Clinical Professor, New York Medical College, Valhalla

Objective: Physicians attending this program will be informed and updated on the recent advances in identifying substance abuse among their patients and treatment; with special emphasis on the neurological and rehabilitative point of view.

2:00 P.M. Effects of Abused Drugs on Memory and Cognition

ANNE GELLER, M.D., New York City

Chief, Smithers Alcoholism Treatment and Training Center, St. Luke's-Roosevelt Hospital Center; Assistant Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons

2:25 P.M. Questions and Answers

2:35 P.M. Cocaine Abuse and its Treatment

ROBERT MILMAN, M.D., New York City

Professor of Psychiatry; Professor of Clinical Public Health, Cornell University Medical College

3:00 P.M. Questions and Answers

3:10 P.M. The Treatment of Chronic Pain

RONALD DOUGHERTY, M.D., Brewerton

Administrative Service Chief, Chemical Abuse Recovery Service, Benjamin Rush Center; Chairman, Drug Abuse Committee, Medical Society of the State of New York

3:35 P.M. Questions and Answers

(continued)

3:45 P.M. Physical Medicine & Rehabilitation: Diagnosis and Therapeutic Rehabilitation in the Alcohol Patient

LAKSHMI MURALI, M.D., New York City

Assistant Director, Rehabilitation Department; Associate Director, Rehabilitation Resident Education Program, St. Vincent's Hospital Medical Center of New York

4:10 P.M. Questions and Answers

4:20 P.M. Alcoholism and Its Neurologic Complications

DAVID GREEN, M.D., Troy

Clinical Professor of Neurology, Albany Medical College of Union University

4:45 P.M.–5:00 P.M. Questions and Answers

Emergency Medicine/Critical Care/Otolaryngology Joint Meeting With New York Chapter of American College of Emergency Physicians New York State Society of Otolaryngology—Head & Neck Surgery New York State Society of Critical Care Medicine, Inc.

2:00 P.M.–5:00 P.M.
GRAMERCY B

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CONTROVERSIES IN THE EMERGENCY DEPARTMENT AND CRITICAL CARE AREAS

LORRAINE M. GIORDANO, M.D., FACEP, Jamaica, *Moderator*

Chairperson, Department of Emergency Medicine, Jamaica Hospital

Objective: This program will acquaint the physician with the controversial issues relating to AIDS victims as well as medical ethics between physician and patient. Current management of adult respiratory distress syndrome and the technique of thoracic aortic balloon occlusion will be presented.

2:00 P.M. Case Presentations on Ethical Issues in the Emergency Department

NEAL FLOMENBAUM, M.D., FACEP, New York City

Assistant Professor of Clinical Medicine, New York University School of Medicine; Associate Director, Emergency Medical Services, Bellevue Hospital Center and New York University Medical Center

3:00 P.M. Intensive Care for AIDS Victims

MARK J. ROSEN, M.D., New York City

Assistant Professor of Medicine, Mount Sinai School of Medicine of the City University of New York; Director, Special Care Unit, Mount Sinai Hospital

3:30 P.M. Controversies in the Management of Adult Respiratory Distress Syndrome

CARLOS R. ORTIZ, M.D., Rochester

Associate Professor of Medicine, University of Rochester School of Medicine and Dentistry; Medical Director, Intensive Care Unit, The Genesee Hospital

4:00 P.M. Upper Airway Management in Trauma

PETER KOLTAI, M.D., Albany

Assistant Professor, Department of Surgery, Division of Otolaryngology, Albany Medical College of Union University

4:30 P.M.–5:00 P.M. Thoracic Aortic Balloon Occlusion: Methods and Indications

WAYNE LONGMORE, M.D., FACEP, Brooklyn

Director of Emergency Services, Brookdale Hospital; Clinical Instructor in Surgery, New York University

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Medical Liability Mutual Insurance Company Joint Meeting With Medical Society of the State of New York

2:00 P.M.–5:00 P.M.
GRAMERCY A

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

LEGAL IMPLICATIONS OF DELAYED DIAGNOSES WITH CASE PRESENTATIONS

(continued)

RALPH M. SCHWARTZ, M.D., New York City, *Moderator*

Associate Professor, Clinical Obstetrics and Gynecology, State University of New York, Health Science Center at Brooklyn; Chairman, Patient Safety Committee, Medical Liability Mutual Insurance Company

Objective: The purpose of this seminar is to provide physicians in attendance with information about professional liability in the practice of medicine. It will deal with cases that appear with some frequency when diagnoses are delayed. Protocols of closed claims will be presented for discussion. It is hoped that this meeting will help to alert the physician to potential hazards and reduce the number of potential liability events by appropriately modifying his practice.

2:00 P.M. Defense and the Plaintiff

DONALD J. FAGER, J.D., New York City

Vice President, Medical Liability Mutual Insurance Company; Partner, Fager and Amsler

2:30 P.M. Defense and the Physician

EDWARD J. AMSLER, J.D., New York City

Assistant Secretary, Medical Liability Mutual Insurance Co.; Partner, Fager and Amsler

3:00 P.M. Obstetrics and Gynecology Problems

JOHN F. DWYER, M.D., New York City

Chairman, Medical Liability Defense Board; Associate Professor, Clinical Obstetrics and Gynecology, New York Medical College

3:30 P.M. Medical Problems Associated with Delayed Medical Diagnoses

KENNETH T. DONALDSON, M.D., Bronx

Consultant in Medicine, St. Luke's-Roosevelt Hospital Center; Associate Clinical Professor in Medicine, Columbia University College of Physicians and Surgeons

4:00 P.M. Surgical Problems Associated with Delayed Medical Diagnoses

JOSEPH FORD, M.D., Bronx

Attending Physician, Surgery, Roosevelt Hospital

4:30 P.M.–5:00 P.M. Panel Discussion

SATURDAY, MARCH 14, 1987

Internal Medicine—Joint Meeting With New York State Society of Internal Medicine

10:00 A.M.–5:00 P.M.
REGENT PARLOR

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 6 Hours, Category 1; AAFP, 6 Hours, Prescribed

POLICING THE PROFESSION: THEM OR US

SIDNEY WEINSTEIN, M.D., Rochester, *Moderator*

Clinical Associate Professor of Medicine, University of Rochester School of Medicine and Dentistry

Objective: To make the physician aware of the function and involvement of both the government and the medical profession in medical discipline and the responsibility of each in this important area.

10:00 A.M. Should We Punish the Ill?

BARTON A. HARRIS, M.D., Lake Success

Medical Director, Committee for Physicians' Health, Medical Society of the State of New York

10:45 A.M. Physician Prescribing and Controlled Substance Abuse

MR. THOMAS COFFEY, JR., Albany

Director, Bureau of Controlled Substances, New York State Department of Health

11:30 A.M. Office of Professional Medical Conduct: Role and Responsibility

MS. KATHLEEN TANNER, Albany

Director, Office of Professional Medical Conduct

12:15 P.M. Panel Discussion

1:00 P.M.–2:00 P.M. Lunch Break

2:00 P.M. Licensure: Status and Standards

WILLIAM JACOTT, M.D., Duluth, Minnesota

President, Federation of State Medical Boards, Duluth Clinic, Lakeside

2:45 P.M. Assessing Clinical Outcome in Quality of Care

DENNIS O'LEARY, M.D., Chicago, Illinois

President, Joint Commission on Accreditation of Hospitals

3:30 P.M. Medicare and Medicaid Fraud and Abuse

KENNETH M. NELSON, M.D., Washington, D.C.

Medical Advisor, Office of Inspector General, Department of Health and Human Services

4:15 P.M.–5:00 P.M. Panel Discussion

(continued)

Ophthalmology
Joint Meeting With
New York State Ophthalmological Society

10:00 A.M.–5:00 P.M.
SUTTON PARLOR CENTER

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 6 Hours, Category 1; AAFP, 6 Hours, Prescribed

GLAUCOMA TREATMENT BY THE PRACTICING OPHTHALMOLOGIST

PATRICIA D. SMITH, M.D., Manhasset, *Moderator*
Physician-in-Charge, Glaucoma, North Shore University Hospital

Objective: To update the practicing ophthalmologist with laser, medical and surgical techniques for management of glaucoma.

10:15 A.M. **Filtering Surgery in General Ophthalmology**
RAYMOND HARRISON, M.D., New York City
Director, Glaucoma Service, Manhattan Eye, Ear and Throat Hospital; Consultant Surgeon, New York Eye and Ear Infirmary

11:00 A.M. **THE LUCIEN HOWE PRIZE: Glaucoma and Cataract**
RICHARD J. SIMMONS, M.D., Boston, Massachusetts
Surgeon, Massachusetts Eye and Ear Infirmary; Associate Clinical Professor, Harvard Medical School

11:45 A.M. **Technique and Complications of Filtering Surgery for Glaucoma**
MAURICE H. LUNTZ, M.D., New York City
Director, Ophthalmology, Beth Israel Medical Center; Clinical Professor of Ophthalmology, Mt. Sinai School of Medicine of the City University of New York

12:30 P.M. **Treatment of Advanced Glaucoma**
MICHAEL E. YABLONSKI, M.D. New York City
Chief, Glaucoma Service; Associate Professor of Clinical Ophthalmology, New York Hospital-Cornell Medical Center

1:00 P.M.–2:00 P.M. **Lunch Break**

2:00 P.M. **Optic Nerve Evaluation for the Practicing Ophthalmologist**
JOSEPH CAPRIOLI, M.D., New Haven, Connecticut
Director, Glaucoma Service, Yale University School of Medicine

2:40 P.M. **Lasers for Glaucoma: LTP Update (Laser Trabecularplasty)**
ARNOLD PRYWES, M.D., Bethpage
Physician-in-Charge, Glaucoma and Allied Disorders, Long Island Jewish Medical Center; Assistant Professor of Ophthalmology, School of Medicine, Health Sciences Center, State University of New York at Stony Brook

3:20 P.M. **Advances in Medical Therapy for Glaucoma**
CARL CAMRAS, M.D., New York City
Assistant Professor of Ophthalmology, Mount Sinai Medical Center

3:40 P.M. **Panel Discussion**
DRS. YABLONSKI, CAMRAS, LUNTZ

4:10 P.M. **Iridectomy: Yag or Argon?**
PATRICIA D. SMITH, M.D., Manhasset

4:30 P.M.–5:00 P.M. **Panel Discussion**
DRS. HARRISON, SMITH, PRYWES

Psychiatry
Joint Meeting With
New York State Psychiatric Association

10:00 A.M.–5:00 P.M.
MURRAY HILL B

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 6 Hours, Category 1; AAFP, 6 Hours, Prescribed

MODERN PSYCHIATRY: CONTROVERSIES, DILEMMAS, QUESTIONS, AND CERTAINTIES

RICHARD B. DROOZ, M.D., New York City, *Moderator*
Associate Professor of Psychiatry (Ret.), State University of New York Health Sciences Center at Brooklyn; Attending Psychiatrist (Ret.), Kings County Hospital Center

(continued)

Objective: The program includes presentations of a wide range of timely subjects for the purpose of placing these areas in theoretical and practical, clinical perspective. In keeping with the overall theme of the three-day meeting, areas of controversy or dilemma will be clearly identified.

10:00 A.M. **The Office Treatment of Depressions**

ROBERT CANCRO, M.D., New York City

Professor and Chairman, Department of Psychiatry, New York University Medical Center; Director, Nathan S. Kline Research Institute, Orangeburg

10:45 A.M. **The Prediction of Dangerousness: Research and Scientism**

JACQUES M. QUEN, M.D., New York City

Clinical Professor of Psychiatry, Cornell University Medical College; Associate Director, Section on the History of Psychiatry, New York Hospital-Cornell Medical Center

11:30 A.M. **The Right to Refuse Treatment in New York: Six Months of Rivers v Katz**

J. RICHARD CICCONE, M.D., Rochester

President, American Academy of Psychiatry and the Law; Associate Professor of Psychiatry, University of Rochester School of Medicine and Dentistry

12:15 P.M. **The Ethical Issues of Peer Review**

ROBERT J. CAMPBELL III, M.D., New York City

Director, Gracie Square Hospital; Editor-in-Chief, *Psychiatric News*, newspaper of the American Psychiatric Association

1:00 P.M.–2:00 P.M. **Lunch Break**

2:00 P.M. **Monoamine Oxidase Inhibitors: Can They Be An Effective Treatment for Cocaine Abuse**

HARVEY R. REDFORD, M.D., Brooklyn

Deputy Director of Psychiatry, Kings County Hospital Center; Clinical Assistant Professor of Psychiatry, State University of New York Health Sciences Center at Brooklyn

2:45 P.M. **Private Practice of Psychiatry: A Model for Survival**

JOHN S. MCINTYRE, M.D., Rochester

Chairperson and Attending Psychiatrist, St. Mary's Hospital; Recorder, Assembly of District Branches, American Psychiatric Association

3:30 P.M. **Assessment of DSM-III Personality Disorders: The Delineation of Psychological Types**

JOHN M. OLDHAM, M.D., New York City

Deputy Director, New York State Psychiatric Institute; Associate Professor of Clinical Psychiatry, Columbia University College of Physicians and Surgeons

4:15 P.M.–5:00 P.M. **Cultural Perspectives in Psychoanalytic Diagnosis and Practice**

WERNER MUENSTERBERGER, Ph.D., New York City

Editor (Ret.), *The Psychoanalytic Study of Society;* Formerly, Associate Professor of Psychiatry, State University of New York Health Sciences Center at Brooklyn

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Hand Surgery/Orthopedic Surgery/Physical Medicine and Rehabilitation Joint Meeting With The New York Society for Surgery of the Hand/The New York Society of Orthopedic Surgery/ The New York Society of Physical Medicine and Rehabilitation

10:00 A.M.–5:00 P.M.
MURRAY HILL A

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 6 Hours, Category 1; AAFP, 6 hours, Prescribed

ARTHRITIS OF THE HAND AND WRIST

THOMAS J. PALMIERI, M.D., New Hyde Park, *Moderator*

Assistant Professor of Clinical Surgery, State University of New York at Stonybrook; Physician-in-Charge, Hand Surgery, Long Island Jewish Medical Center

Objective: To provide the internist, rheumatologist, primary care physician, and orthopedic, plastic and hand surgeon, as well as therapists, nurses, and paramedical personnel with an update on the dilemmas and controversies in treating patients with arthritis of the hand and wrist.

10:00 A.M. **Etiology and Pathogenesis of Rheumatoid and Osteoarthritis of the Hand and Wrist**

HARRY SPIERA, M.D., New York City

Clinical Professor of Medicine; Chief, Division of Rheumatology, Mount Sinai School of Medicine of the City University of New York

(continued)

10:30 A.M. **The Examination and Differential Diagnosis of Arthroses of the Hand and Wrist**

ROY KULICK, M.D., New York City

Assistant, Orthopedic Surgery, Montefiore Hospital and Medical Center, Bronx; Associate Attending, Orthopedic Surgery, Doctors Hospital

11:00 A.M. **The Value of Diagnostic Procedures: X-Rays, Blood Tests, Synovial Fluid Analysis**

HERBERT DIAMOND, M.D., New Hyde Park

Chairman, Department of Medicine, Long Island Jewish-Hillside Medical Center; Professor of Medicine, State University of New York at Stonybrook Health Sciences Center

11:30 A.M. **The Choice and Pharmacology of Nonsteroidal Anti-inflammatory Agents in the Treatment of Arthritis**

DOUGLAS J. MUND, M.D., Great Neck

Assistant Professor of Clinical Medicine, State University of New York at Stony Brook Health Sciences Center; Staff Physician, Long Island Jewish Medical Center

12:00 NOON **Choosing a Disease Modifying Anti-rheumatic Drug (Gold, Anti-malarial, penicillamine, azathioprine, methotrexate and other medications)**

ROBERT M. MARCUS, M.D., Massapequa

Assistant Professor of Clinical Medicine, State University of New York at Stonybrook; Member, Board of Trustees, Arthritis Foundation

12:30 P.M. **Surgical Procedures for the Relief of Pain and Preservation of Function of the Hand and Wrist**

JOSEPH LEDDY, M.D., New Brunswick, New Jersey

Clinical Associate Professor of Surgery, Division of Orthopedics, Department of Surgery; Director, Hand Surgery (Orthopedics), University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School; Chief, Division of Orthopedics; Chief, Hand Surgery, St. Peter's Medical Center

1:00 P.M.–2:00 P.M. **Lunch Break**

2:00 P.M. **The Wrist in Rheumatoid Arthritis**

ROBERT E. CARROLL, M.D., New York City

Professor of Orthopedic Surgery, Columbia University College of Physicians and Surgeons; Director, Hand Surgery, Columbia-Presbyterian Medical Center

2:30 P.M. **Rheumatoid Deformities of the Metacarpophalangeal and Proximal Interphalangeal Joints**

THOMAS J. PALMIERI, M.D., New Hyde Park

3:00 P.M. **Rheumatoid Arthritis of the Thumb**

CHITRANJAN RANAWAT, M.D., New York City

Professor of Orthopedic Surgery, Cornell University Medical College—The New York Hospital and the Hospital for Special Surgery; Attending Orthopedic Surgeon; Director, Hand Service, the Hospital for Special Surgery

3:30 P.M. **Osteoarthritis of the Hand and Wrist**

MARTIN A. POSNER, M.D., New York City

Associate Clinical Professor of Orthopedic Surgery, Mt. Sinai School of Medicine of the City University of New York; Chief, Hand Service, Mt. Sinai Hospital, Lenox Hill Hospital, and the Hospital for Joint Diseases, Orthopedic Institute

4:00 P.M. **Miscellaneous Arthroses of the Hand and Wrist: Lupus Erythematosus, Psoriasis, Scleroderma, Gout, and Infectious Arthritis**

ALLAN E. INGLIS, M.D., New York City

Professor of Clinical Surgery; Professor of Clinical Anatomy in In-Cell Biology and Anatomy, Cornell University Medical College

4:30 P.M.–5:00 P.M. **Hand Therapy and Splinting for the Arthritic Hand and Wrist**

FAYE GRAND, O.T.R., Little Neck

Senior Hand Therapist, Hand Rehabilitation Center of Long Island, New Hyde Park; Director, Hand Therapy Center

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Urology/Pathology
Joint Meeting With
New York State Urological Society
New York State Society of Pathology

10:00 A.M.–1:00 P.M.
NASSAU A

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

PROSTATE CARCINOMA: DIAGNOSIS, STAGING AND CURRENT TRENDS IN TREATMENT

PETER J. PUCHNER, M.D., New York City, *Moderator*

Associate Attending Urologist, Columbia Presbyterian Medical Center; Associate Professor of Clinical Urology, Columbia University College of Physicians and Surgeons

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and

NATHAN S. TAYLOR, M.D., Rochester, *Co-Moderator*

Pathologist, Rochester General Hospital; Assistant Clinical Professor of Pathology, University of Rochester School of Medicine and Dentistry

Objective: This joint symposium is presented on the most common carcinoma in older men. Attendees will be informed of the important principles in the diagnosis and staging of the cancer, which will be discussed by a panel including experts in pathology, urology, radiotherapy, and oncology.

10:00 A.M. **The Histologic Diagnosis of Prostate Carcinoma**

JOHN F. GAETA, M.D., Buffalo

Chief of Pathology, Roswell Park Memorial Institute; Professor of Pathology, State University of New York at Buffalo

10:25 A.M. **Fine Needle Aspiration Diagnosis of Prostate Carcinoma**

JERRY WAISMAN, M.D., New York City

Director of Laboratories, University Hospital; Professor of Pathology, New York University Medical Center

10:45 A.M. **Clinical Staging of Prostate Carcinoma**

MITCHELL C. BENSON, M.D., New York City

Assistant Attending Urologist, Presbyterian Hospital; Assistant Professor of Urology, Columbia University College of Physicians and Surgeons

11:05 A.M. **Surgical Treatment of Prostate Carcinoma**

CARL A. OLSSON, M.D., New York City

Professor and Chairman, Department of Urology, Columbia University College of Physicians and Surgeons

11:30 A.M. **Radiation Therapy for Prostate Carcinoma: External Beam versus Interstitial Treatment**

JAMES D. COX, M.D., New York City

Professor and Chairman, Department of Radiation Oncology, Presbyterian Hospital, Columbia University College of Physicians and Surgeons

11:55 A.M. **Medical Therapy for Prostate Cancer**

ALLAN YAGODA, M.D., New York City

Department of Medicine, Section of Urologic Oncology, Memorial Sloan-Kettering Cancer Center

12:20 P.M. **Controversies in the Treatment of Prostate Carcinoma Panel Discussion:**

DRS. JAMES D. COX, MITCHELL C. BENSON, CARL A. OLSSON and ALLAN YAGODA

12:45 P.M.–1:00 P.M. **Questions and Answers**

Dermatology
Joint Meeting With
New York State Society of Dermatology

10:00 A.M.–1:00 P.M.
NASSAU B

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CURRENT PROBLEMS OF AIDS AND UPDATE ON SKIN CANCER

EUGENE L. BODIAN, M.D., Great Neck, *Moderator*

Chief, Division of Dermatology, North Shore University Hospital; Clinical Professor of Medicine, Cornell University Medical College

Objective: This program will deal with problems of AIDS, with new concepts of diagnosis, treatment, and will also have an update on skin cancer by one of the leaders in this field. A panel of management and labor will address the clinical dilemmas facing dermatologists created by HMO's and the liability crisis.

10:00 A.M. **Dermatological Relationship to Organized Labor Today**

MR. GUS TYLER, New York City

Assistant to the President, International Ladies Garment Workers Union

10:35 A.M. **Questions and Answers**

10:45 A.M. **AIDS: What's New In Diagnosis, Therapy, Prognosis, and Research**

MARK KAPLAN, M.D., Manhasset

Chief, Division of Infectious Disease, North Shore University Hospital; Professor of Medicine, Cornell University Medical College

11:20 A.M. **Questions and Answers**

11:30 A.M. **HMO Deception: A Dermatological Dilemma**

MR. LEWIS BOXENBAUM, New York City

President, Brown, Boxenbaum, Inc.

12:05 P.M. **Questions and Answers**

12:15 P.M. **A. WALTER SUTTER LECTURESHIP FUND: Skin Cancer: Malignant Melanoma Update**

ALFRED KOPF, M.D., New York City

Professor of Dermatology, Skin and Cancer Unit, New York University

12:50 P.M.–1:00 P.M. **Questions and Answers**

(continued)

Computers in Medicine

2:00 P.M.–5:00 P.M.
MADISON SUITE

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

PRACTICAL USES OF COMPUTERS IN MEDICAL AND SURGICAL PRACTICE

LAWRENCE B. TILIS, M.D., Pittsford, *Moderator*

President, American Physicians Association of Computer Medicine, Inc.; Attending Physician, Rochester General Hospital and Park Ridge Hospital

Objective: Hands on education of the physicians in the selection and use of computer systems for billing, practice management, medical records as relates to quality of care.

2:00 P.M. **Telecommunications in Medicine: Basis and Techniques Expanding the Use of Computers in Medicine**

WILLIAM WEISSMAN, M.D., New York City

President, Theorex Corporation; Adjunct Research Professor, New Jersey Institute of Technology

3:30 P.M.–5:00 P.M. **Computerized Medical Billing, Practice Management and Medical Records**

LAWRENCE B. TILIS, M.D., Pittsford

Terrorism and Medicine

2:00 P.M.–5:00 P.M.
SUTTON PARLOR SOUTH

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

TERRORISM: ITS CAUSES AND EFFECTS

MAXWELL SPRING, M.D., Bronx, *Moderator*

Associate Chairman, Scientific Program Committee, Medical Society of the State of New York; Clinical Associate Professor of Medicine, New Jersey Medical School of the University of Medicine and Dentistry of New Jersey

Objective: The physician will gain a greater understanding of the social, medical and psychological causes and effects of political terrorism and how it may effect his/her medical practice.

2:00 P.M. **Terrorism: Its Origin and Development**

Police Officer CHARLES PAGANI, Bronx

Retired Police Officer, Emergency Service Unit, New York City Police Department

3:00 P.M. **Questions and Answers**

3:15 P.M. **The Mind of the Terrorist: Individual, Group and Organizational Dynamics of Political Terrorism**

JERROLD M. POST, M.D., Bethesda, Maryland

Director, Political and Military Psychology, Defense Systems, Inc. (DSI); Associate Clinical Professor of Psychiatry and Behavioral Sciences, George Washington University

4:15 P.M. **Questions and Answers**

4:30 P.M. **Speaker to be Announced**

4:50 P.M.–5:00 P.M. **Questions and Answers**

(continued)

SUNDAY, MARCH 15, 1987

Allergy and Immunology

10:00 A.M.–1:00 P.M.
MURRAY HILL B

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

FOOD ALLERGY UPDATE

Objective: There is an explosion of books on various aspects of food allergy aimed at the lay public. The purpose of this course is to bring the knowledge of the practicing physician in this area up-to-date and to delineate accepted methods of managing food allergy from quackery.

10:00 A.M. Introduction

YALAMANCHILI A. K. RAO, M.D., Brooklyn

Assistant Director, Department of Allergy and Immunology, The Long Island College Hospital; Assistant Professor of Clinical Medicine, State University of New York Health Science Center at Brooklyn

10:05 A.M. Food Allergy: Fact or Fad!

WILLIAM J. DAVIS, M.D., New York City

Director, Division of Allergy; Associate Professor, Pediatrics, Columbia Presbyterian Medical Center

10:35 A.M. Clinical Manifestations and Diagnosis

LAWRENCE T. CHIARAMONTE, M.D., Brooklyn

Director, Department of Allergy and Immunology, The Long Island College Hospital; Assistant Professor of Clinical Medicine, State University of New York Health Science Center at Brooklyn

11:05 A.M. Unusual Manifestations of Food Allergy

JOHN CONDEMI, M.D., Rochester

Professor of Medicine, University of Rochester School of Medicine and Dentistry

11:35 A.M. Food Additives and Preservatives

ARLENE T. SCHNEIDER, M.D., Brooklyn

Associate Director, Department of Allergy and Immunology; Assistant Professor, Clinical Medicine, State University of New York Health Science Center at Brooklyn

12:05 P.M. Controversial Methods in Managing Food Allergy

MICHAEL H. GRIECO, M.D., New York City

Chief, Division of Allergy and Clinical Immunology; Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons

12:35 P.M.–1:00 P.M. Panel Discussion

General Surgery/Radiology/Anesthesiology
Joint Meeting With
NYS Society of Surgeons/NYS Chapter of the American College of Radiology/ NYS Society of Anesthesiologists

10:00 A.M.–1:00 P.M.
MURRAY HILL A

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

STATE OF THE ART OF THE MANAGEMENT OF BREAST CANCER

LESLIE WISE, M.D., New Hyde Park, *Moderator*

Professor and Chairman, Department of Surgery, Long Island Jewish Medical Center; Professor of Surgery, State University of New York at Stonybrook

Objective: To acquaint physicians with the current state of the art in management of breast cancer, highlighting different diagnostic and therapeutic approaches.

10:00 A.M. The Primary Treatment for Operable Breast Cancer

LESLIE WISE, M.D.

10:40 A.M. Questions and Answers

10:45 A.M. Lumpectomy VS Mastectomy: The Cost of Breast Preservation for Cancer

ERIC MUNOZ, M.D., M.B.A., New Hyde Park

Head, Research Division, Department of Surgery, Long Island Jewish Medical Center

11:05 A.M. Questions and Answers

(continued)

11:10 A.M. **Multimodalities in the Diagnosis of Early Breast Cancer**

RITA F. GIROLAMO, M.D., Valhalla

Professor of Radiology, New York Medical College; Director of Mammography, Westchester County Medical Center

11:35 A.M. **Questions and Answers**

11:40 A.M. **Conservative Management of Early Breast Cancer**

CHITTI MOORTHY, M.D., Valhalla

Associate Professor of Radiology; Director, Radiation Oncology, New York Medical College

12:10 P.M. **Questions and Answers**

12:15 P.M. **Anesthesia for the Morbidly Obese**

NANCY SCHREIBER, M.D., East Meadow

Director, Resident Education; Associate Medical Director, Respiratory Therapy, Nassau County Medical Center

12:55 P.M.–1:00 P.M. **Questions and Answers**

Obstetrics and Gynecology/Women's Medical Society of New York State Joint Meeting With American College of Obstetrics-Gynecology District II

10:00 A.M.–1:00 P.M.
GRAMERCY B

CONTINUING MEDICAL EDUCATION CREDIT: AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

OBSTETRICS AND GYNECOLOGY AND WOMEN'S MEDICINE

JOHN T. PARENTE, M.D., Bronx, *Moderator*

Director, Department of Obstetrics and Gynecology, Bronx-Lebanon Hospital Center; Associate Professor, Obstetrics and Gynecology, Albert Einstein College of Medicine of Yeshiva University

Objective: To point out the important and critical subjects relating to obstetricians and gynecologists and their patients.

10:00 A.M. **AIDS in Pregnancy**

RICHARD SCHWARZ, M.D., Brooklyn

Professor and Chairman, Department of Obstetrics and Gynecology, State University of New York Health Science Center at Brooklyn

11:00 A.M. **The Role of the Obstetrician-Gynecologist in the Diagnosis and Treatment of Breast Disease**

DOUGLAS J. MARCHANT, M.D., Boston, Massachusetts

Professor, Obstetrics and Gynecology; Professor, Surgery, Tufts University of Medicine

12:00 NOON–1:00 P.M. PATRICIA NUMANN, M.D., Syracuse, *Moderator*

State Director, American Medical Women's Association

12:00 NOON **Abortion: Safety in the State of New York**

SALLY DORFMAN, M.D., Bronx

Assistant Professor of Obstetrics and Gynecology; Director, Family Planning Program, Development and Research, Albert Einstein College of Medicine of Yeshiva University

Discussant:

SHELLEY J. SHERMAN, Esq., New York City

Deputy Counsel, Office of Professional Medical Conduct, New York State Department of Health

12:30 P.M.–1:00 P.M. **Women and Smoking**

LESLIE J. KOHMAN, M.D., Syracuse

Assistant Professor of Surgery, State University of New York Health Science Center at Syracuse

(continued)

Family Practice/Orthopedic Surgery
Joint Meeting With
NYS Academy of Family Physicians/NYS Society of Orthopedic Surgery

10:00 A.M.–1:00 P.M.
NASSAU A

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CLINICAL SKILLS IN DIAGNOSIS

MARK H. KROTOWSKI, M.D., Brooklyn, *Moderator*

Clinical Assistant Professor of Family Practice, State University of New York Health Science Center at Brooklyn

MAXWELL SPRING, M.D., Bronx, *Co-Moderator*

Associate Chairman, Scientific Program Committee, Medical Society of the State of New York; Clinical Associate Professor of Medicine, New Jersey Medical School

Objective: This program is meant to familiarize the family physician with areas of clinical diagnosis which confront the primary care physician almost daily.

10:00 A.M. **Orthopedic Neurology as Related to Back Pain: Clinical Evaluation for Office Use**

STANLEY HOPPENFELD, M.D., Bronx

Associate Clinical Professor of Orthopedic Surgery, Albert Einstein College of Medicine of Yeshiva University

11:00 A.M.–1:00 P.M. **The Clinical Art of Cardiac Auscultation: An Audio Presentation**

JULES CONSTANT, M.D., Buffalo

Clinical Associate Professor of Medicine and Cardiology, State University of New York at Buffalo School of Medicine

---

Neurosurgery

10:00 A.M.–1:00 P.M.
MORGAN SUITE

CONTINUING MEDICAL EDUCATION CREDIT:
AMA, PRA, 3 Hours, Category 1; AAFP, 3 Hours, Prescribed

CONTROVERSIES IN NEUROSURGERY

KALMON D. POST, M.D., New York City, *Moderator*

Associate Professor of Neurological Surgery, Columbia University College of Physicians and Surgeons

Objective: To update neurosurgeons in the management of three controversial areas.

10:00 A.M. **Arterial Infusion Therapy on Gliomas**

JOHN P. KAPP, M.D., Ph.D., Buffalo

Professor and Chairman, Department of Neurosurgery, State University of New York at Buffalo

10:40 A.M. **Questions and Answers**

11:00 A.M. **An Update for Surgical Treatment of Malignant Glioma**

PAUL KORNBLITH, M.D., Bronx

Professor and Chairman of the Leo Davidoff Department of Neurosurgery, Albert Einstein College of Medicine of Yeshiva University

11:40 A.M. **Questions and Answers**

12:00 NOON **Controversies in Carotid Artery Surgery**

DONALD O. QUEST, M.D., New York City

Associate Professor of Neurosurgery, Columbia University College of Physicians and Surgeons

12:40 P.M.–1:00 P.M. **Questions and Answers**

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Capital Resource Associates — **Booth 26**
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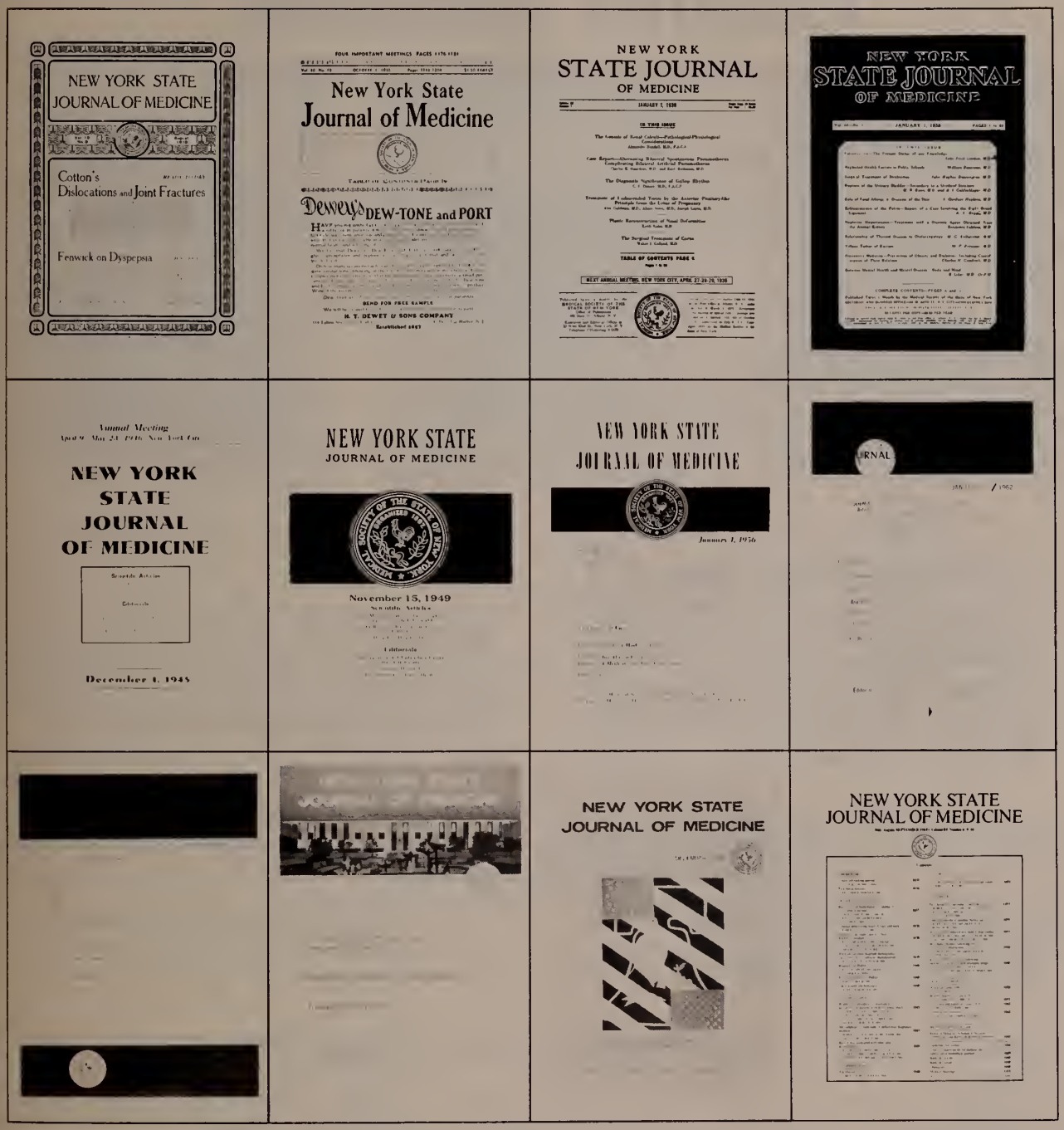

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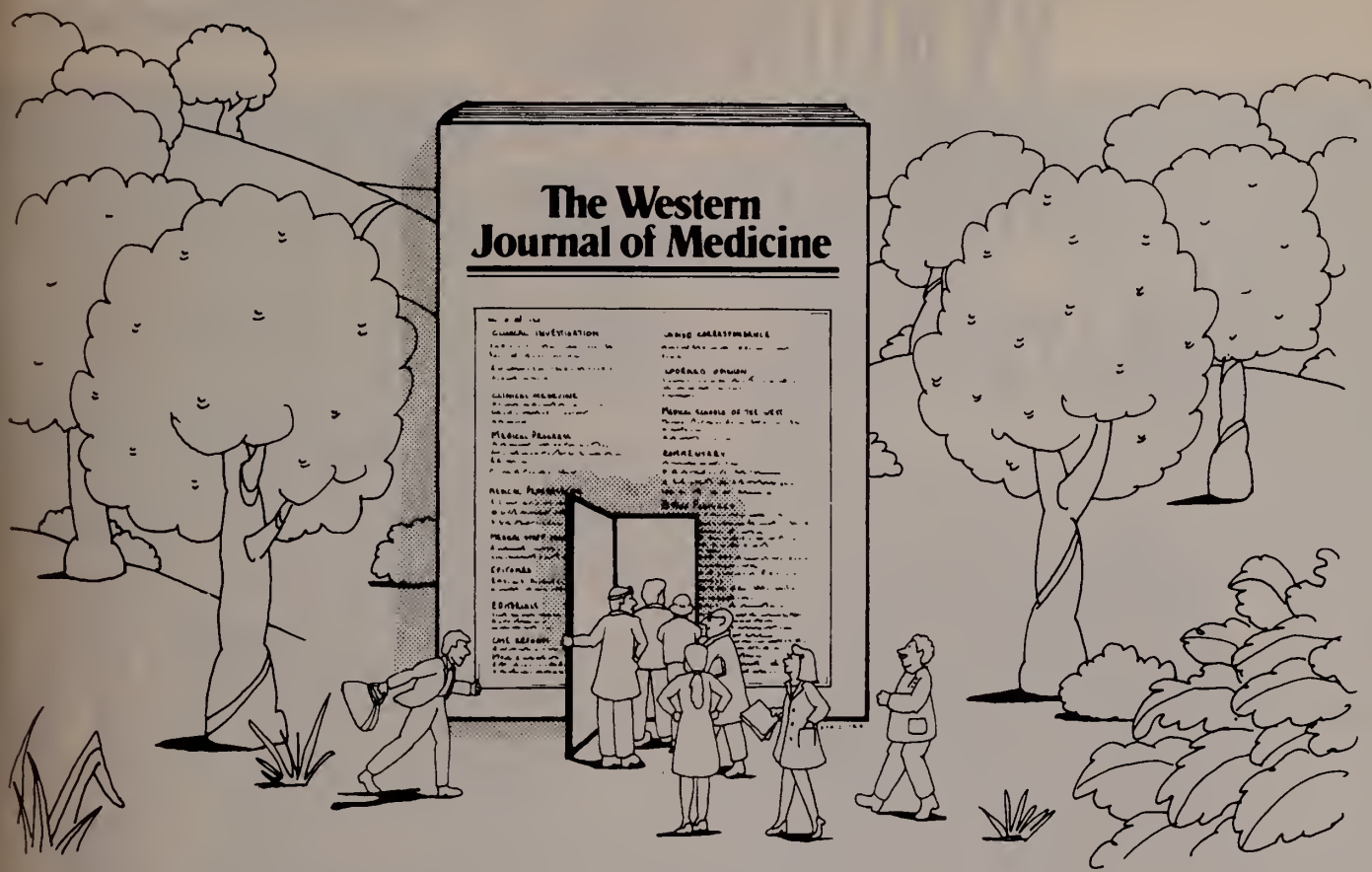

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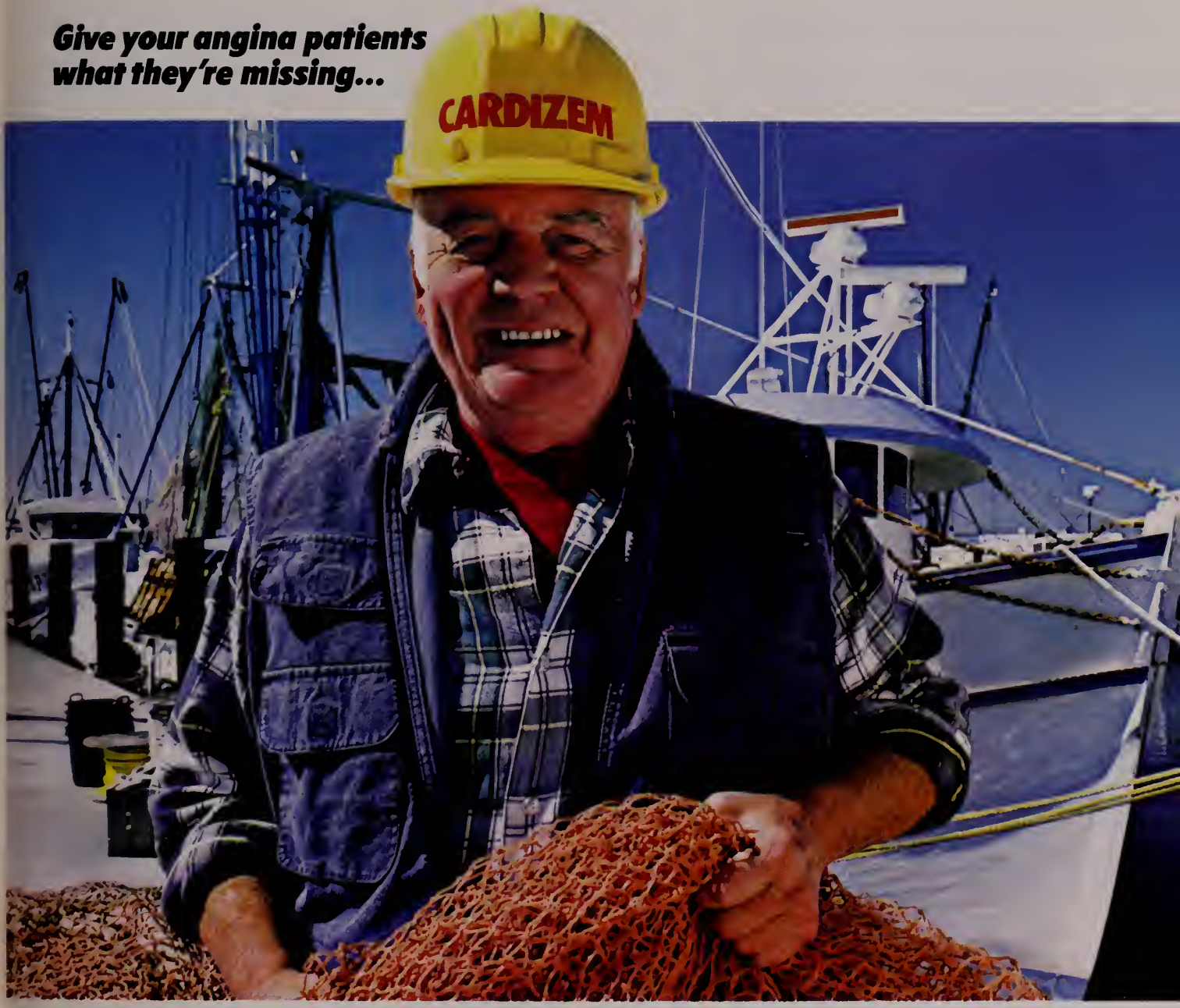

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CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS
General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

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See complete Professional Use Information before prescribing.

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For criteria on admission and referrals, please contact the Medical Director, at 1-212-307-0735. Spellman is a division of St. Clare's Hospital and Health Center, designated the first AIDS treatment center by New York State.

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